

## Large-scale genotyping identifies 41 new loci associated with breast cancer risk

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### Supplementary Note

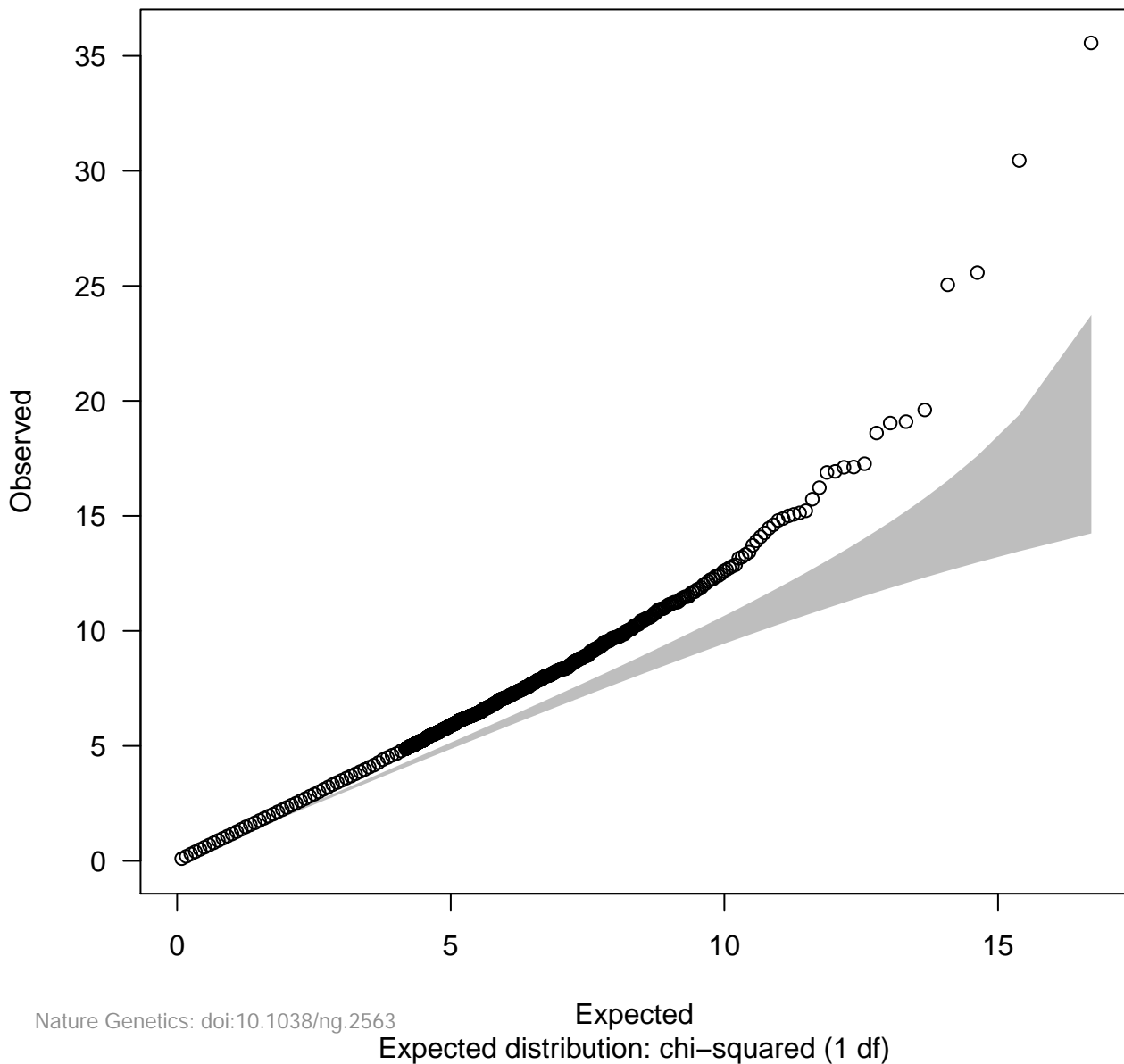
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## Supplementary Figures

**Supplementary Figure 1(a)** Quantile-quantile plot for 22,897 uncorrelated iCOGS SNPs selected by consortia other than BCAC. **(b)** Quantile-quantile plot for 29,807 iCOGS SNPs selected from the combined GWAS analysis and not located in regions previously known to be associated with breast cancer.

(a)

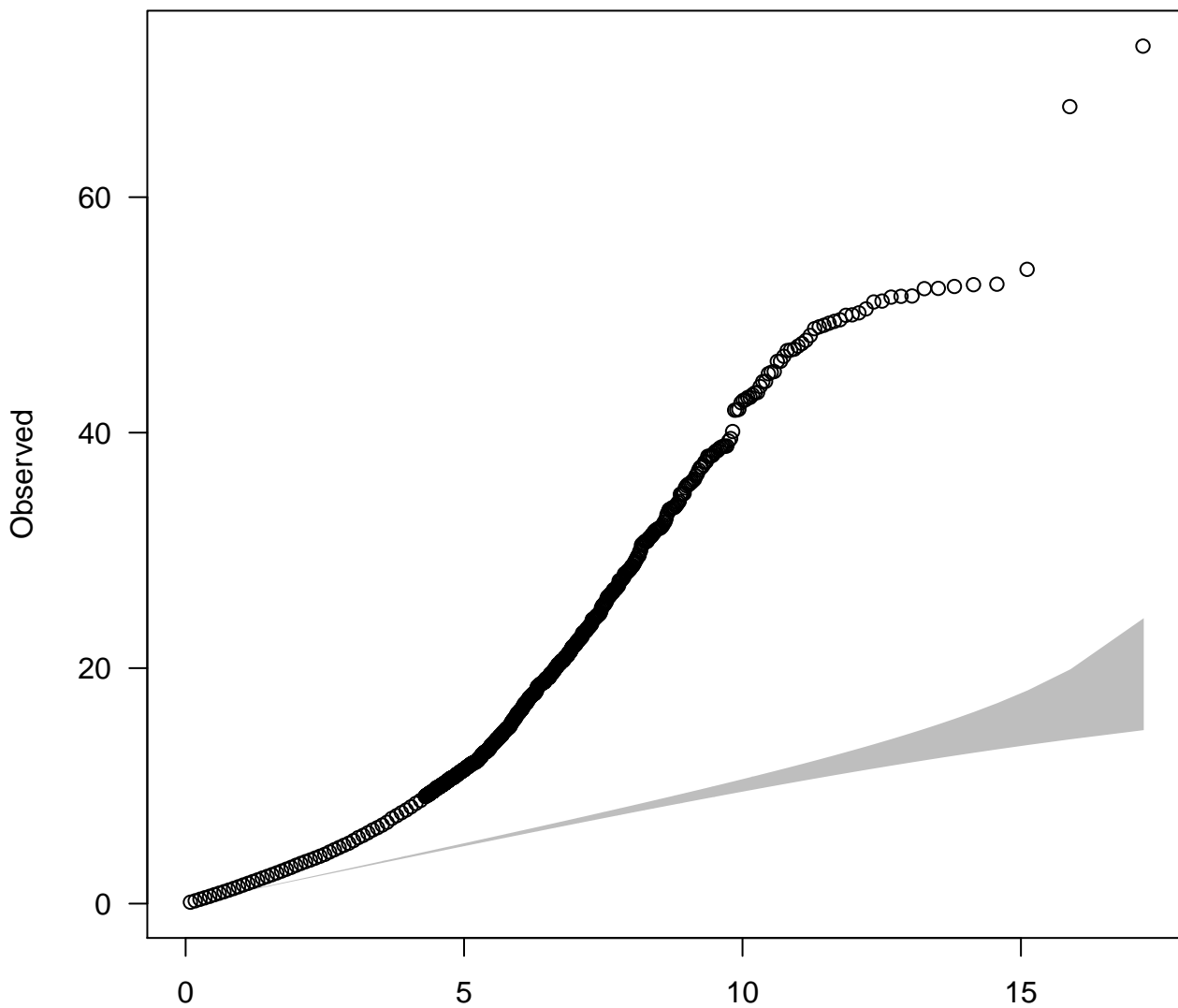
# QQ plot



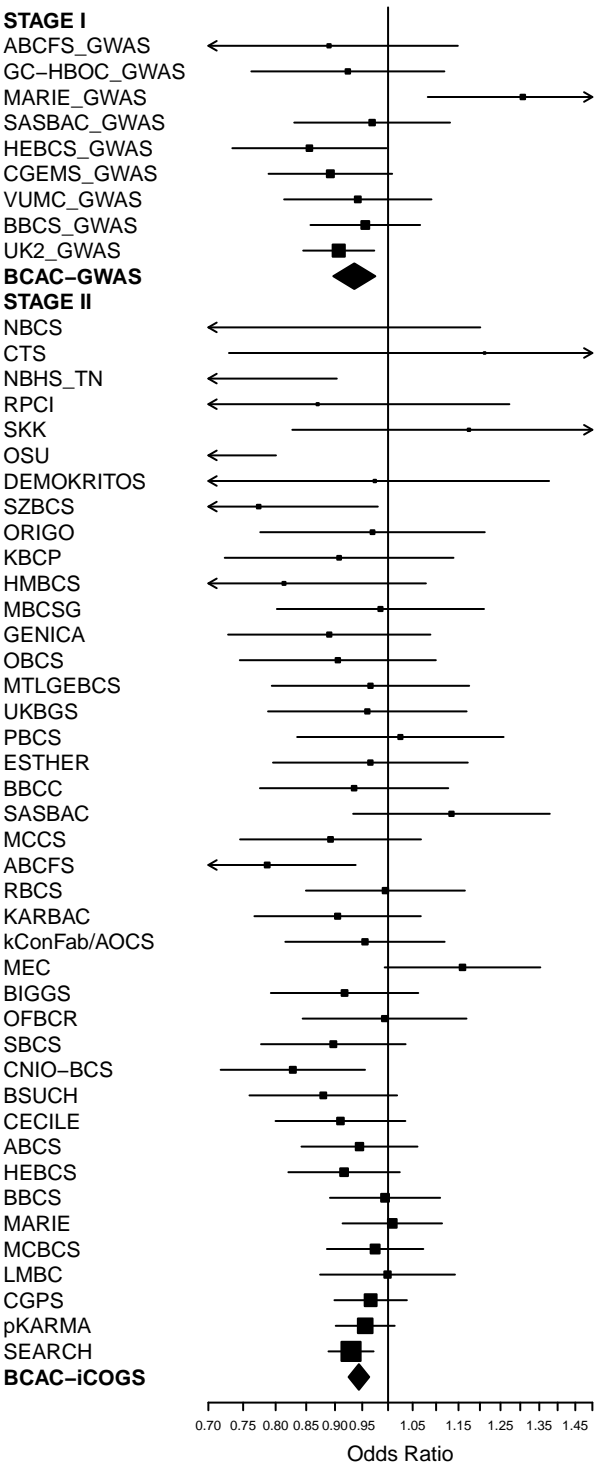


(b)

# QQ plot



**Supplementary Figure 2.** Forest plots for 41 loci achieving genome-wide significance. Squares denote the estimated per-allele OR for the minor allele in Europeans. The horizontal lines denote 95% confidence limits. The area of the square is inversely proportional to the variance of the estimate. The diamond denotes the estimated per-allele OR from the combined analysis in BCAC.



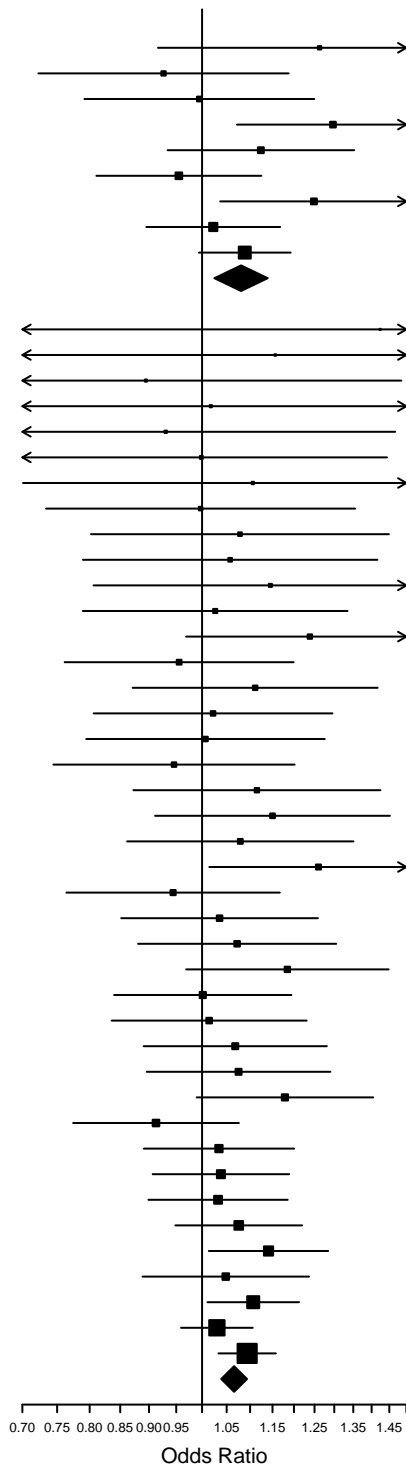
p-het iCOGS=0.13  
I<sup>2</sup> iCOGS=20.47

**STAGE I**

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



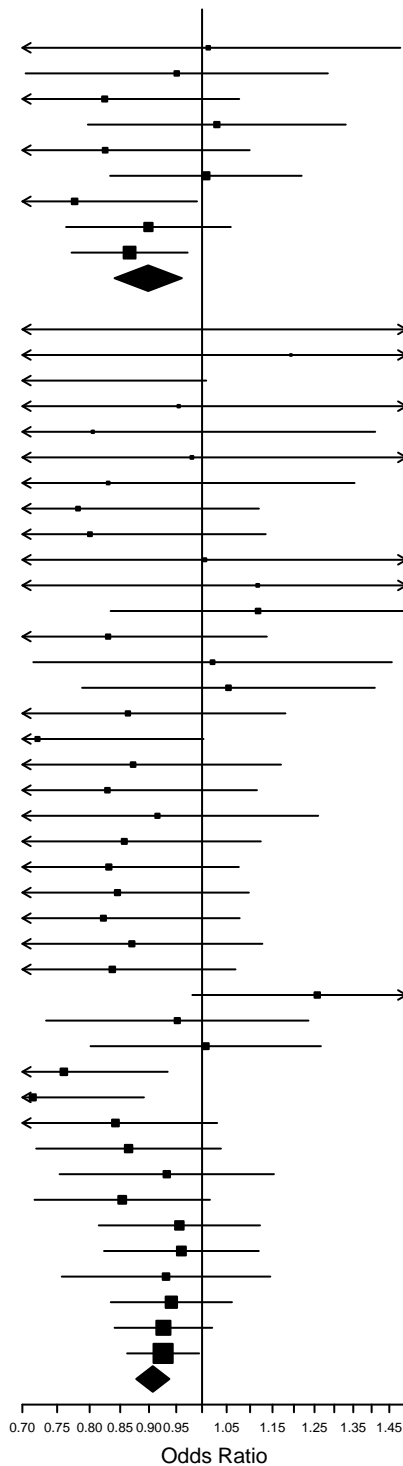
p-het iCOGS=0.995  
 $I^2$  iCOGS=0

**STAGE I**

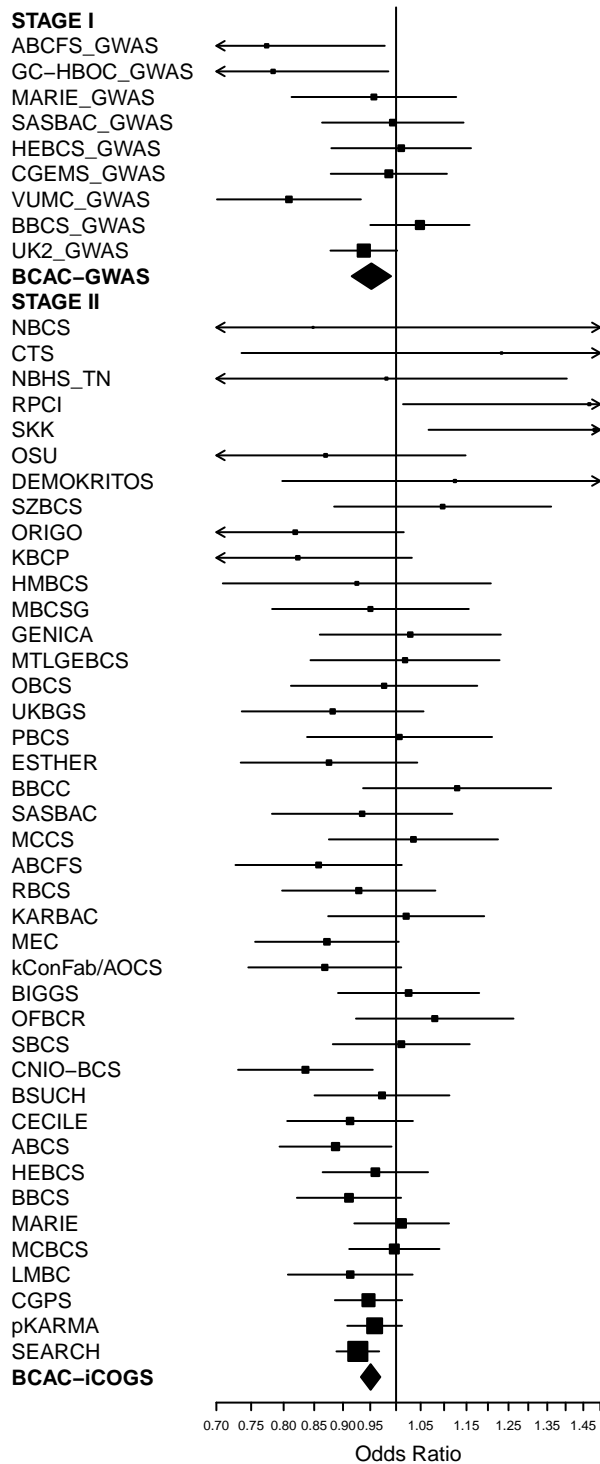
ABCFS\_GWAS  
 GC-HBOC\_GWAS  
 MARIE\_GWAS  
 SASBAC\_GWAS  
 HEBCS\_GWAS  
 CGEMS\_GWAS  
 VUMC\_GWAS  
 BBCS\_GWAS  
 UK2\_GWAS

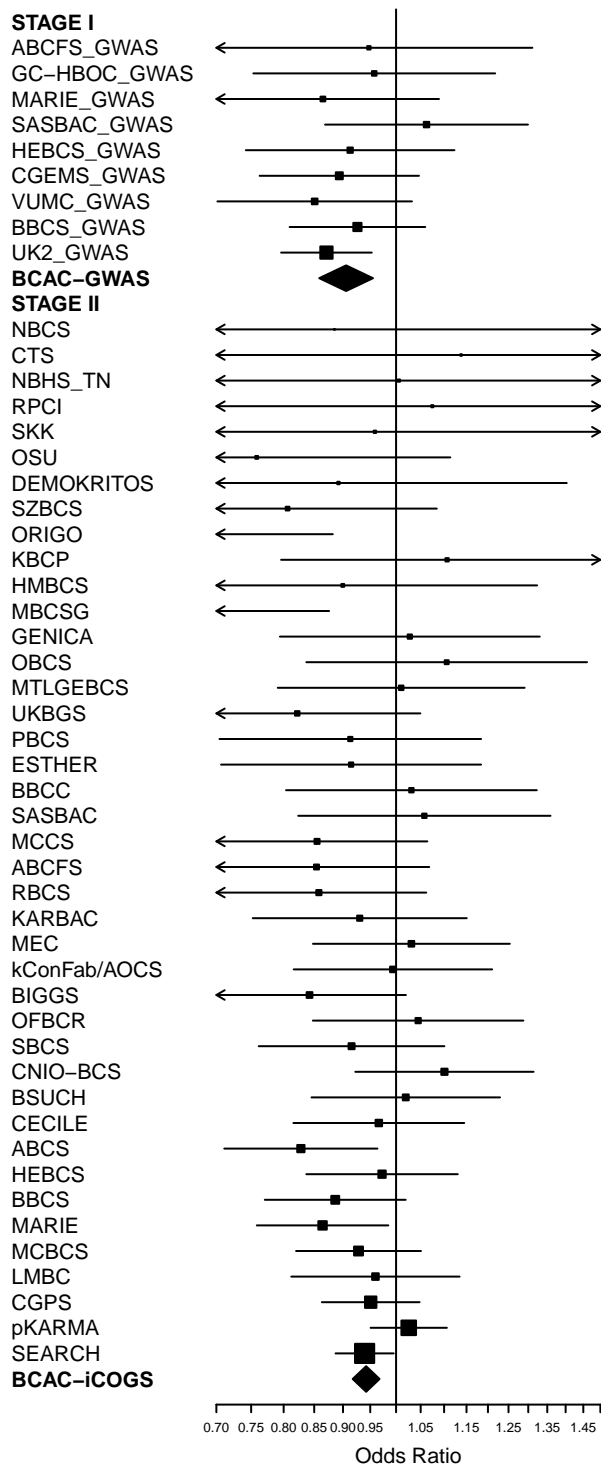
**BCAC-GWAS****STAGE II**

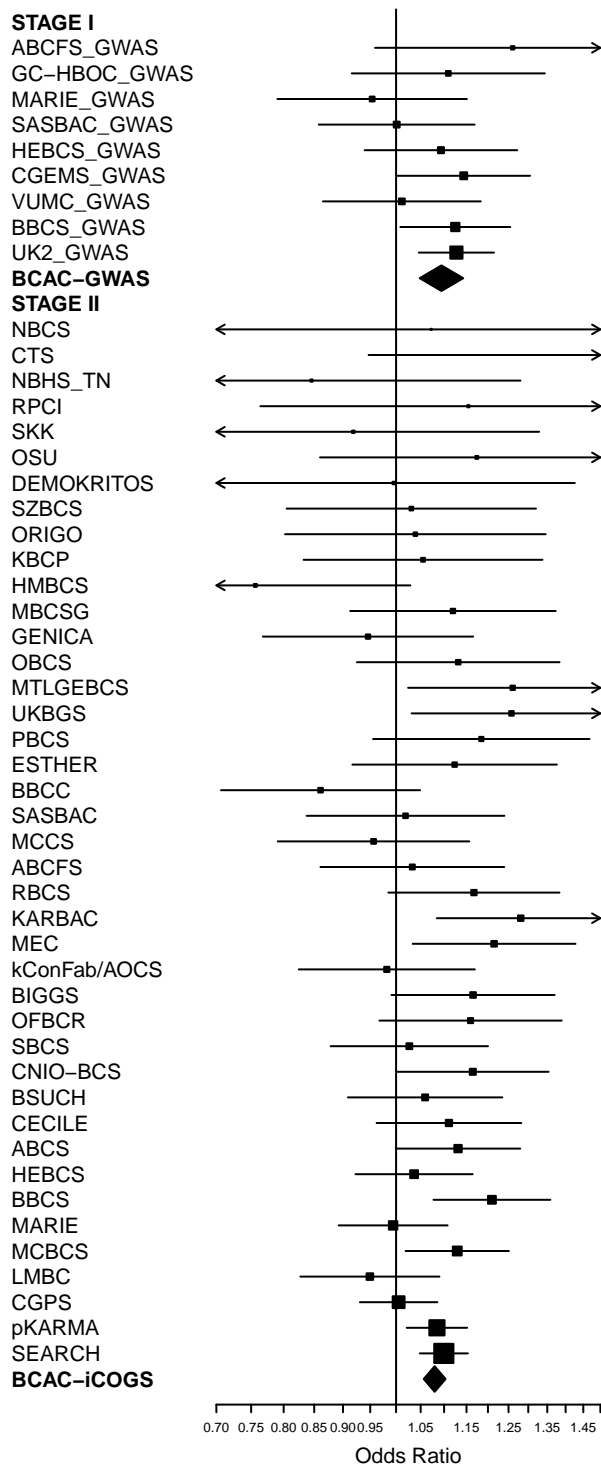
NBCS  
 CTS  
 NBHS\_TN  
 RPCI  
 SKK  
 OSU  
 DEMOKRITOS  
 SZBCS  
 ORIGO  
 KBCP  
 HMBCS  
 MBCSG  
 GENICA  
 OBCS  
 MTLGEBCS  
 UKBGS  
 PBCS  
 ESTHER  
 BBCC  
 SASBAC  
 MCCS  
 ABCFS  
 RBCS  
 KARBAC  
 kConFab/AOCS  
 MEC  
 BIGGS  
 OFBCR  
 SBSCS  
 CNIO-BCS  
 BSUCH  
 CECILE  
 ABCS  
 HEBCS  
 BBCS  
 MARIE  
 MCBCS  
 LMBC  
 CGPS  
 pKARMA  
 SEARCH  
**BCAC-iCOGS**



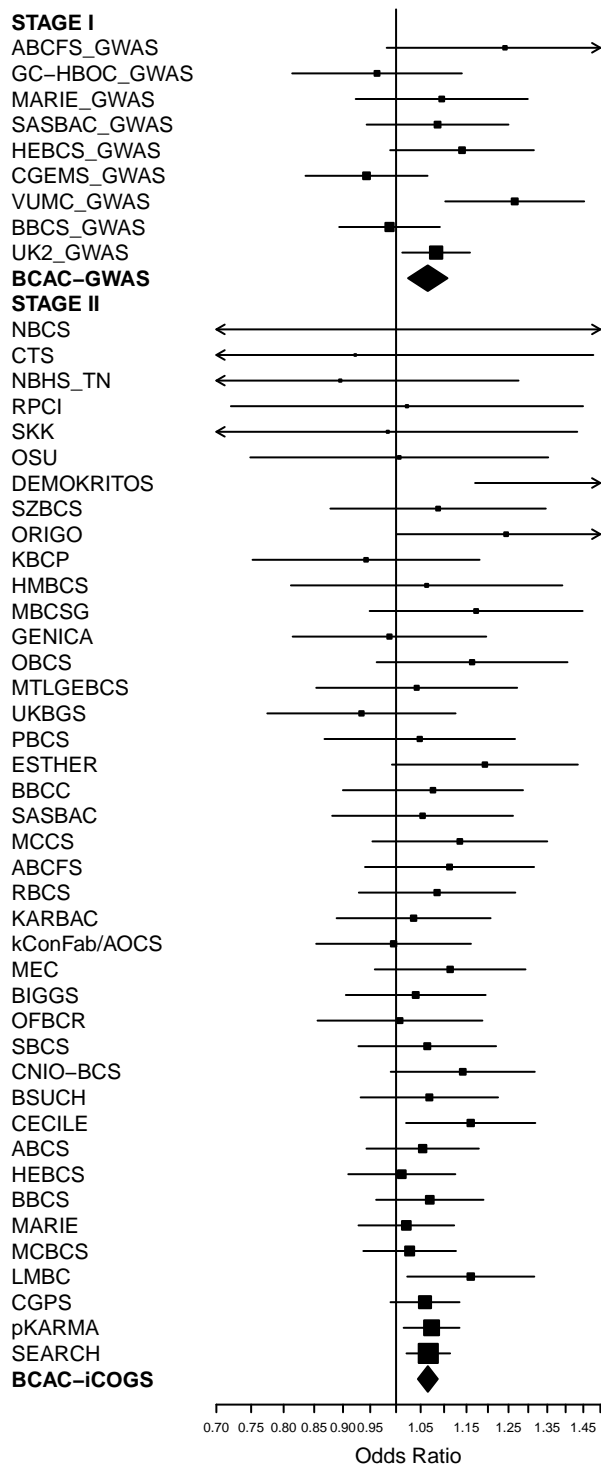
p-het iCOGS=0.78  
 $I^2$  iCOGS=0











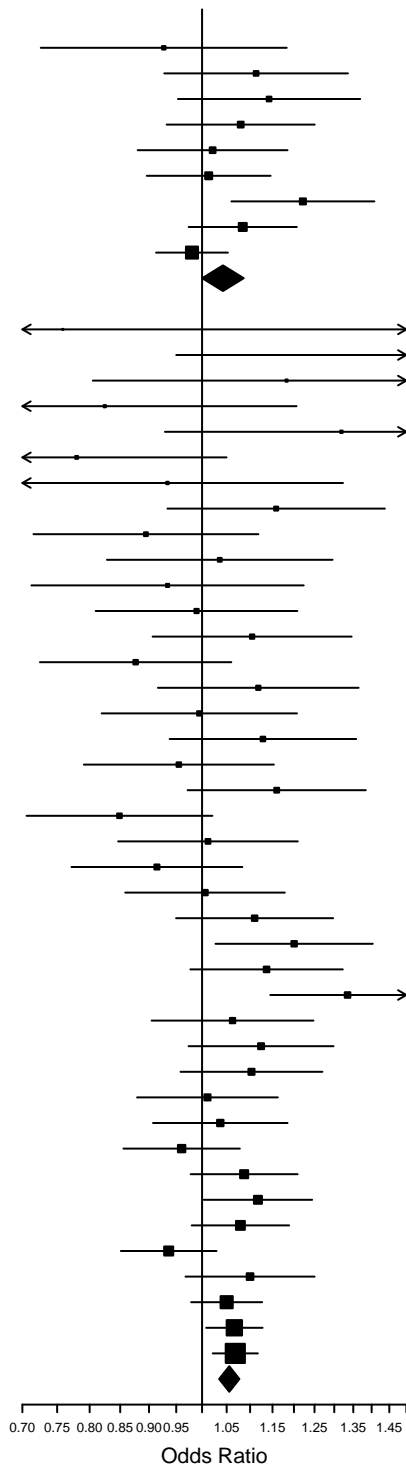
p-het iCOGS=0.81  
I^2 iCOGS=0

**STAGE I**

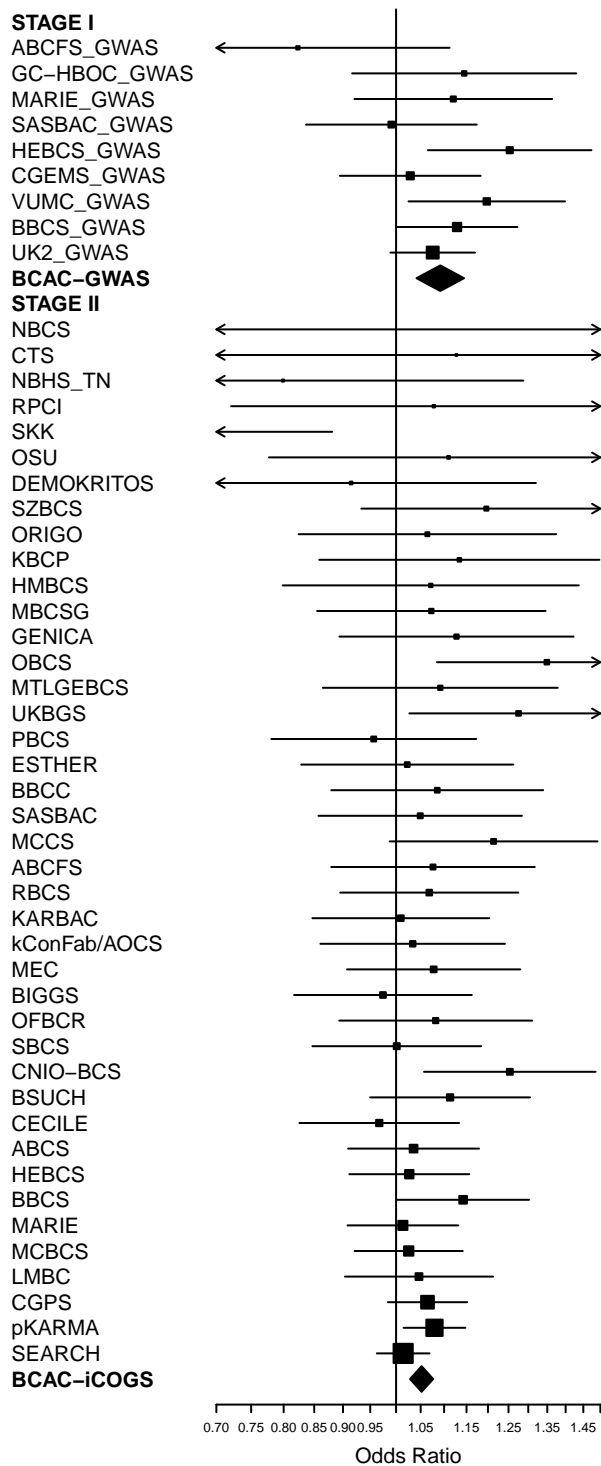
ABCFS\_GWAS  
 GC-HBOC\_GWAS  
 MARIE\_GWAS  
 SASBAC\_GWAS  
 HEBCS\_GWAS  
 CGEMS\_GWAS  
 VUMC\_GWAS  
 BBCS\_GWAS  
 UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
 CTS  
 NBHS\_TN  
 RPCI  
 SKK  
 OSU  
 DEMOKRITOS  
 SZBCS  
 ORIGO  
 KBCP  
 HMBCS  
 MBCSG  
 GENICA  
 OBCS  
 MTLGEBCS  
 UKBGS  
 PBCS  
 ESTHER  
 BBCC  
 SASBAC  
 MCCS  
 ABCFS  
 RBCS  
 KARBAC  
 kConFab/AOCS  
 MEC  
 BIGGS  
 OFBCR  
 SBCS  
 CNIO-BCS  
 BSUCH  
 CECILE  
 ABCS  
 HEBCS  
 BBCS  
 MARIE  
 MCBCS  
 LMBC  
 CGPS  
 pKARMA  
 SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.03  
 $I^2$  iCOGS=31.01



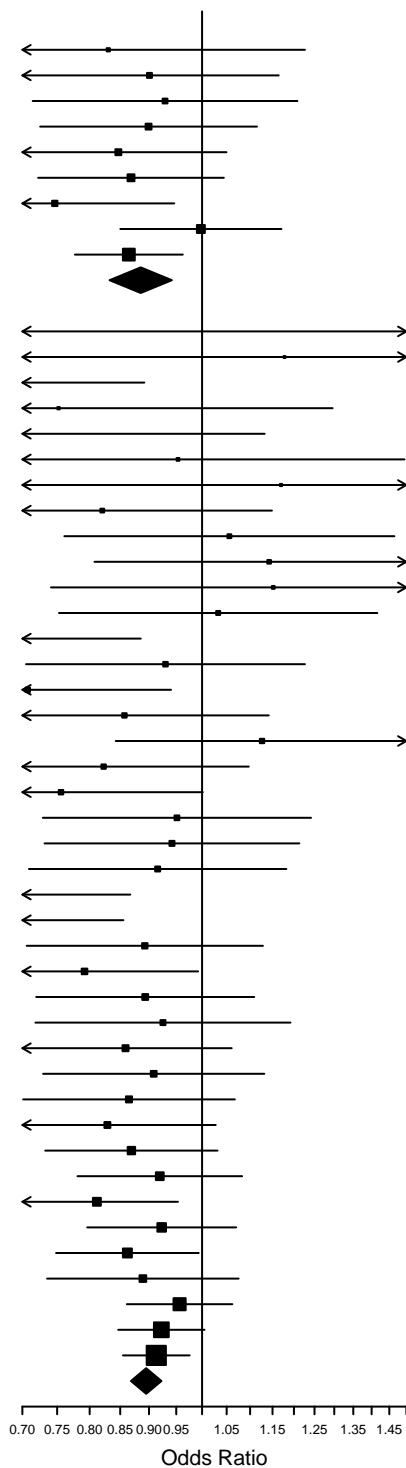
p-het iCOGS=0.42  
I<sup>2</sup> iCOGS=2.67

**STAGE I**

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



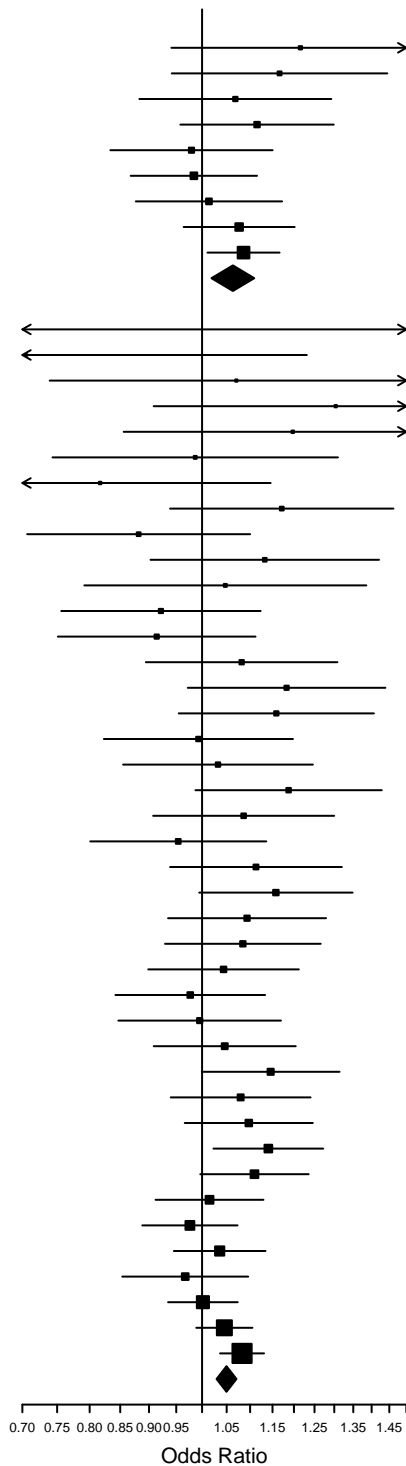
p-het iCOGS=0.54  
 $I^2$  iCOGS=0

**STAGE I**

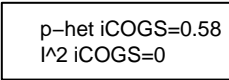
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

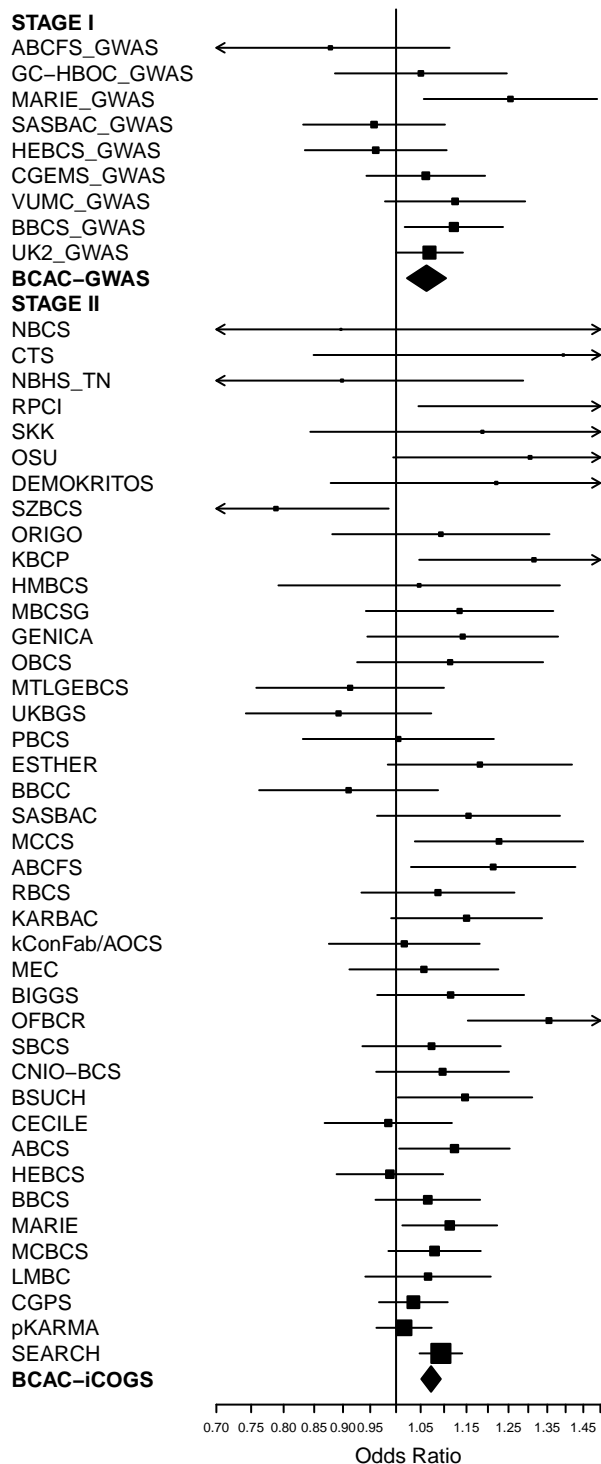
**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.42  
I<sup>2</sup> iCOGS=2.75



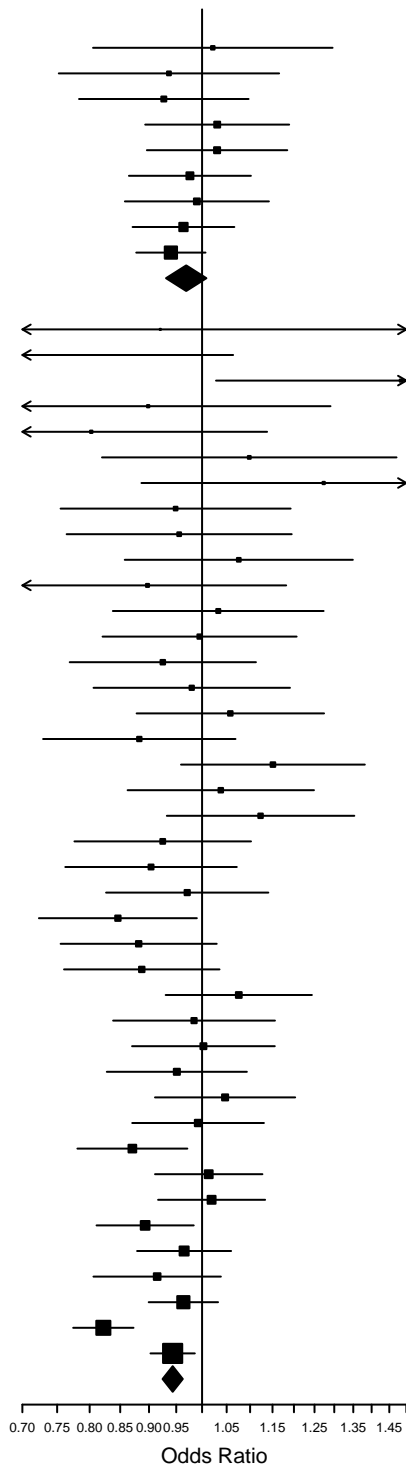


**STAGE I**

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

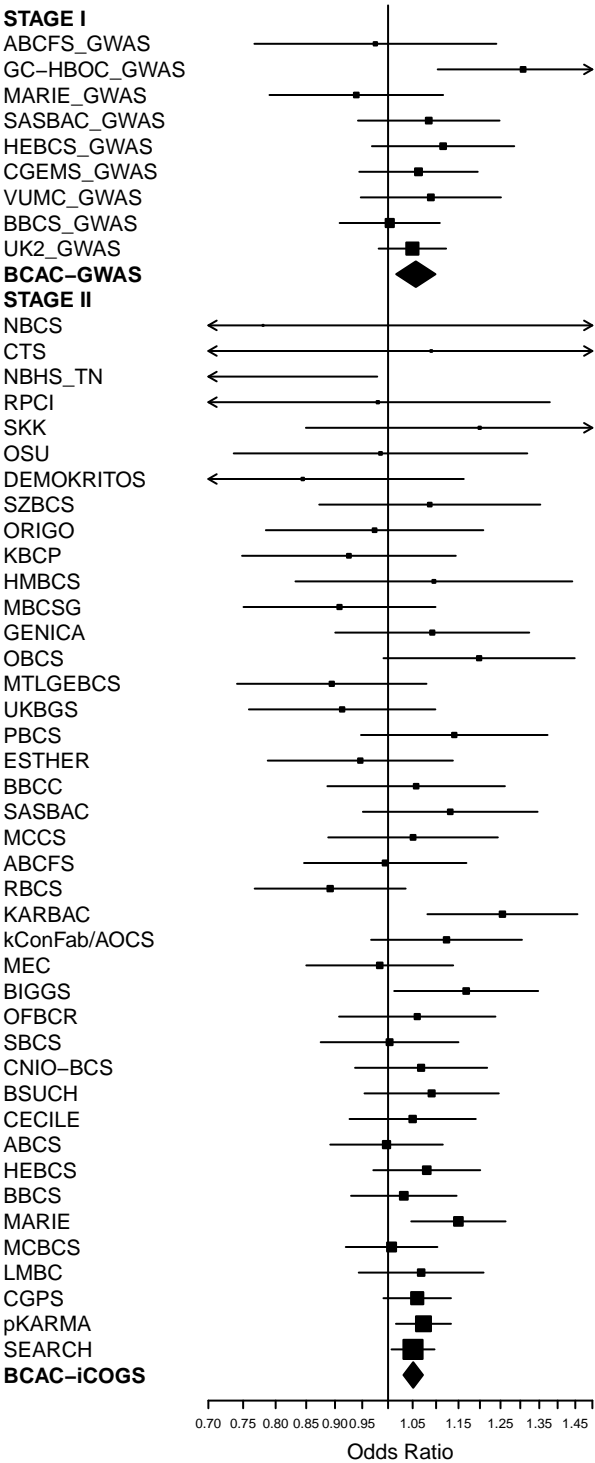
**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**

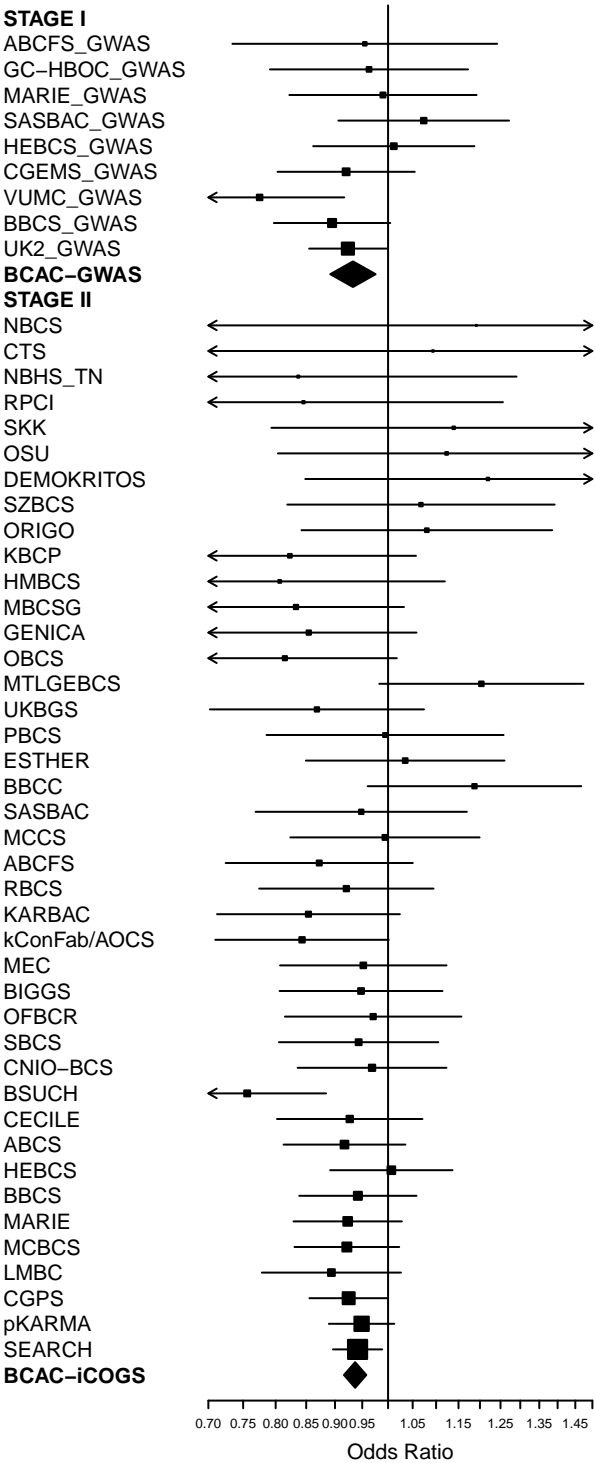


p-het iCOGS=0.01  
 $I^2$  iCOGS=37.05

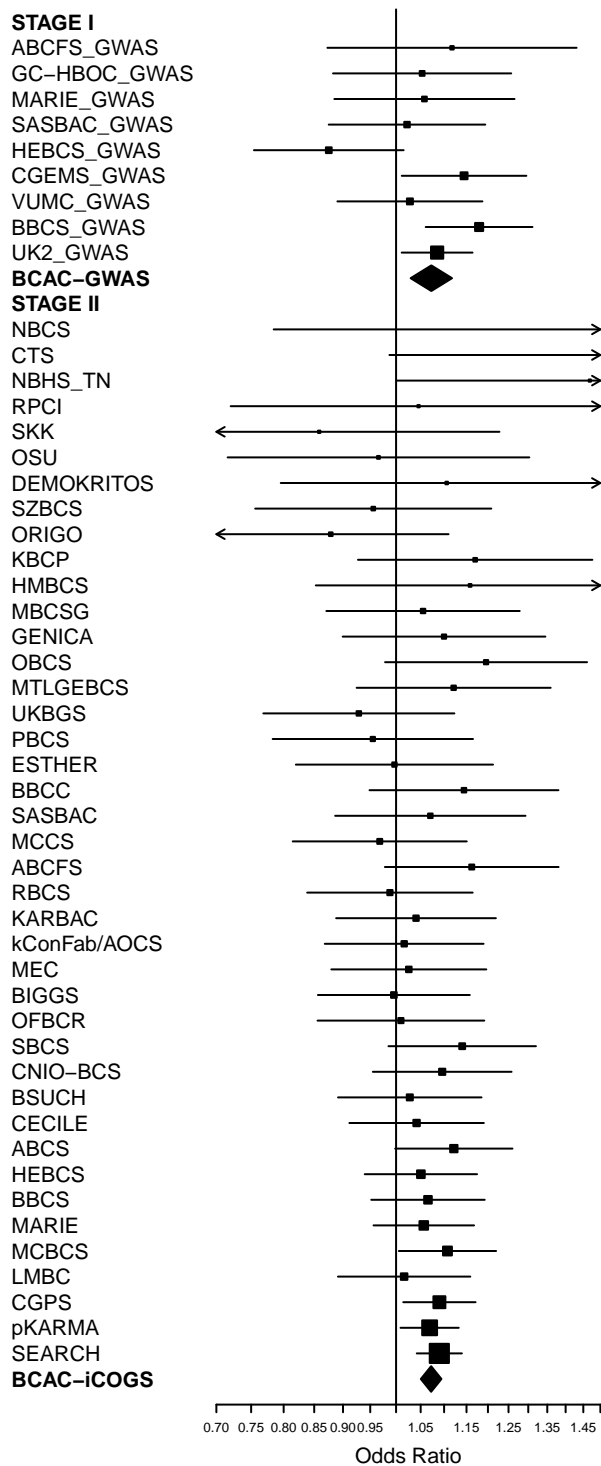




p-het iCOGS=0.37  
I<sup>2</sup> iCOGS=5.69



p-het iCOGS=0.37  
I<sup>2</sup> iCOGS=5.46



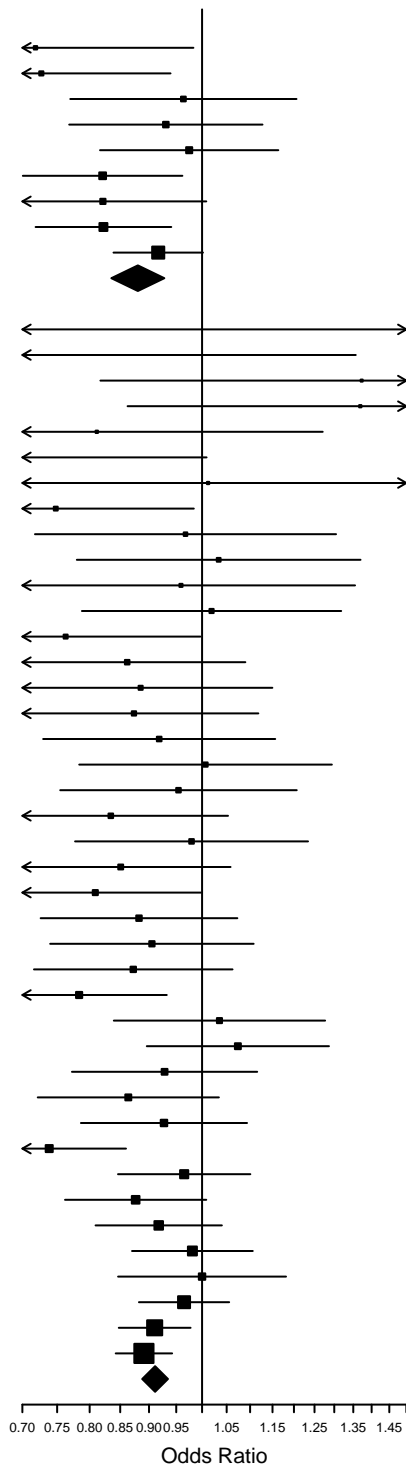
p-het iCOGS=0.93  
I^2 iCOGS=0

**STAGE I**

ABCFS\_GWAS  
 GC-HBOC\_GWAS  
 MARIE\_GWAS  
 SASBAC\_GWAS  
 HEBCS\_GWAS  
 CGEMS\_GWAS  
 VUMC\_GWAS  
 BBCS\_GWAS  
 UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
 CTS  
 NBHS\_TN  
 RPCI  
 SKK  
 OSU  
 DEMOKRITOS  
 SZBCS  
 ORIGO  
 KBCP  
 HMBCS  
 GENICA  
 MBCSG  
 OBCS  
 MTLGEBCS  
 UKBGS  
 PBCS  
 ESTHER  
 BBCC  
 SASBAC  
 MCCS  
 ABCFS  
 RBCS  
 KARBAC  
 MEC  
 kConFab/AOCS  
 BIGGS  
 OFBCR  
 SBSCS  
 CNIO-BCS  
 BSUCH  
 CECILE  
 ABCS  
 HEBCS  
 BBCS  
 MARIE  
 MCBSCS  
 LMBC  
 CGPS  
 pKARMA  
 SEARCH  
**BCAC-iCOGS**



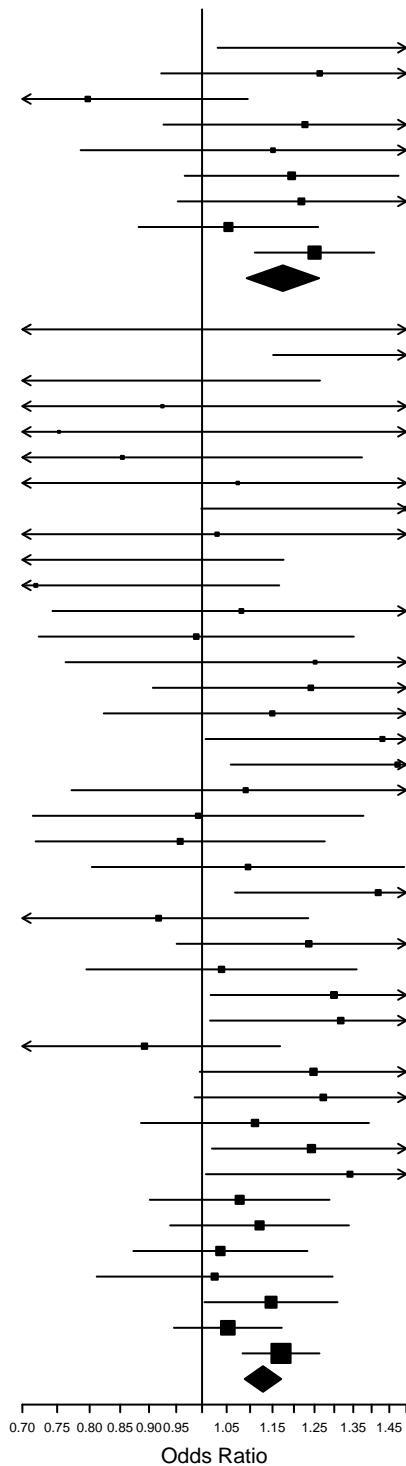
p-het iCOGS=0.64  
 $I^2$  iCOGS=0

**STAGE I**

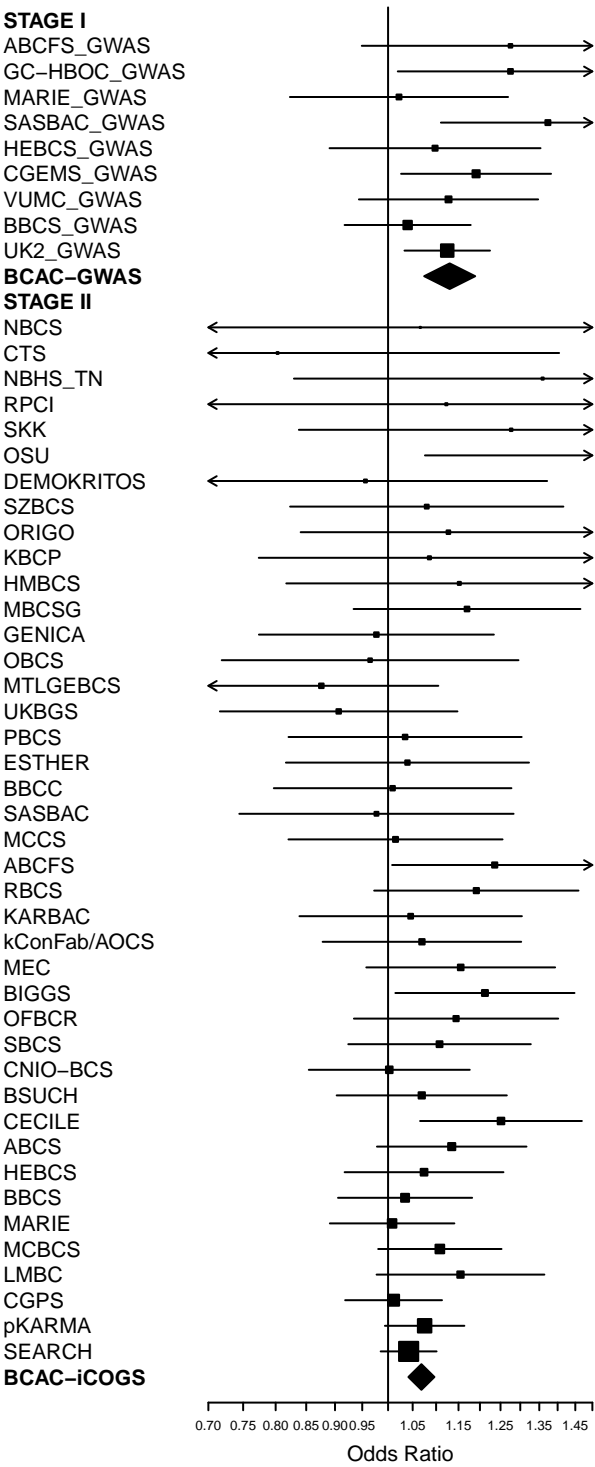
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
GENICA  
MBCSG  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
SASBAC  
BBCC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
SBCS  
OFBCR  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.26  
 $I^2$  iCOGS=11.9

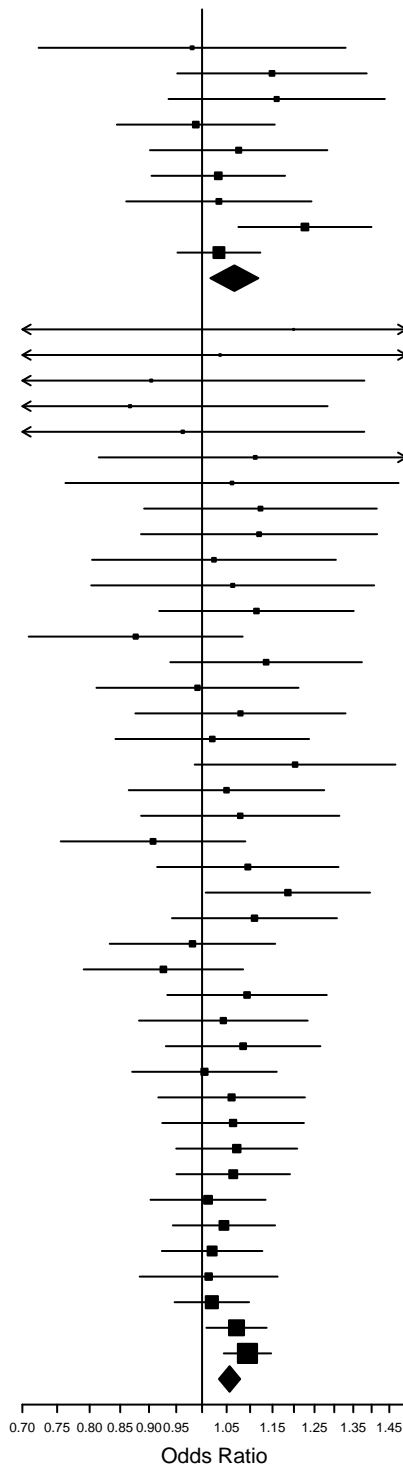


**STAGE I**

ABCFS\_GWAS  
 GC-HBOC\_GWAS  
 MARIE\_GWAS  
 SASBAC\_GWAS  
 HEBCS\_GWAS  
 CGEMS\_GWAS  
 VUMC\_GWAS  
 BBCS\_GWAS  
 UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
 CTS  
 NBHS\_TN  
 RPCI  
 SKK  
 OSU  
 DEMOKRITOS  
 SZBCS  
 ORIGO  
 KBCP  
 HMBCS  
 MBCSG  
 GENICA  
 OBCS  
 MTLGEBCS  
 UKBGS  
 PBCS  
 ESTHER  
 BBCC  
 SASBAC  
 MCCS  
 ABCFS  
 RBCS  
 KARBAC  
 kConFab/AOCS  
 MEC  
 BIGGS  
 OFBCR  
 SBCS  
 CNIO-BCS  
 BSUCH  
 CECILE  
 ABCS  
 HEBCS  
 BBCS  
 MARIE  
 MCBCS  
 LMBC  
 CGPS  
 pKARMA  
 SEARCH  
**BCAC-iCOGS**



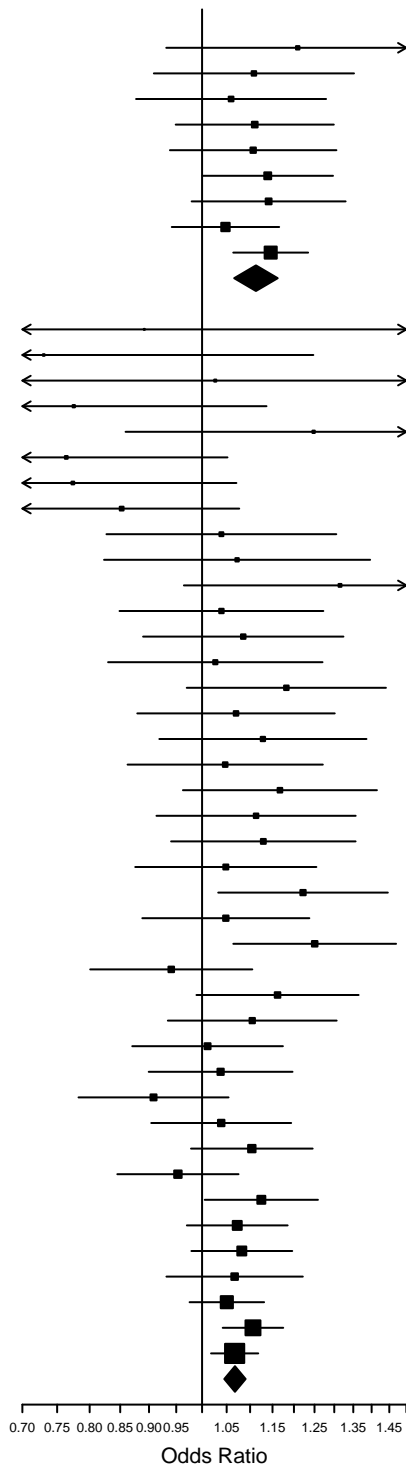
$p\text{-het iCOGS}=0.93$   
 $I^2 \text{ iCOGS}=0$

**STAGE I**

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

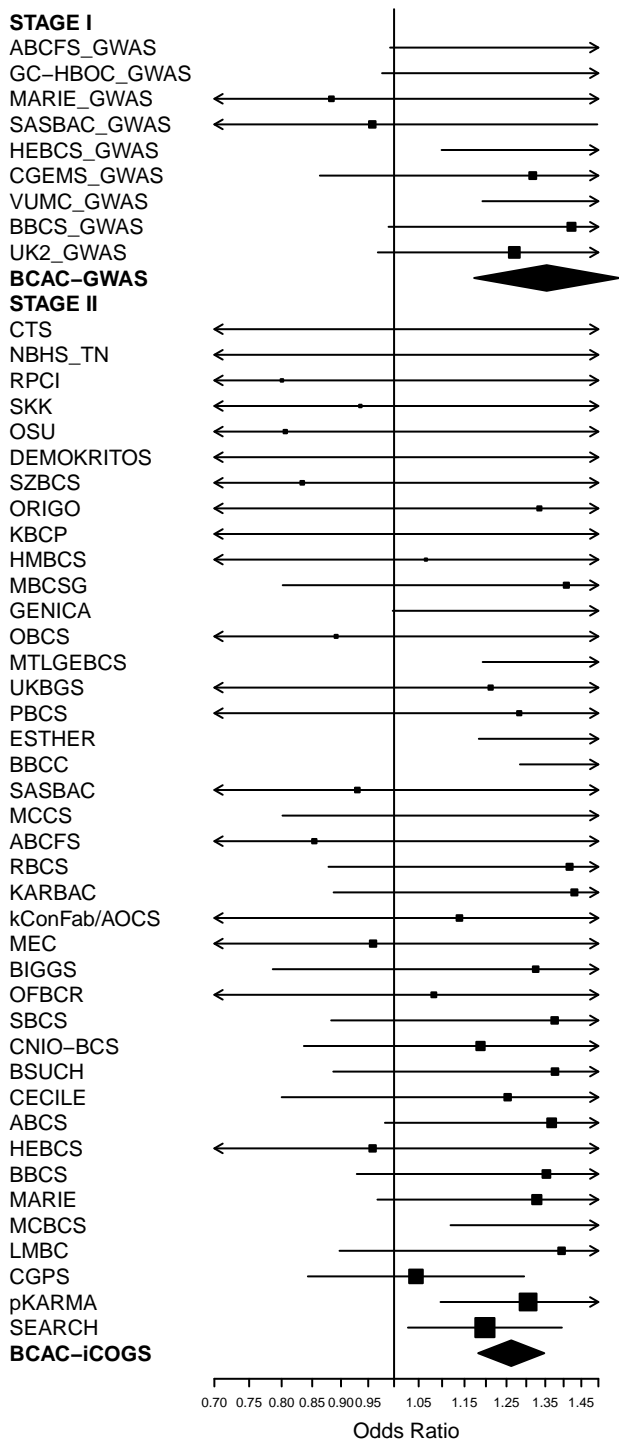
**BCAC-GWAS****STAGE II**

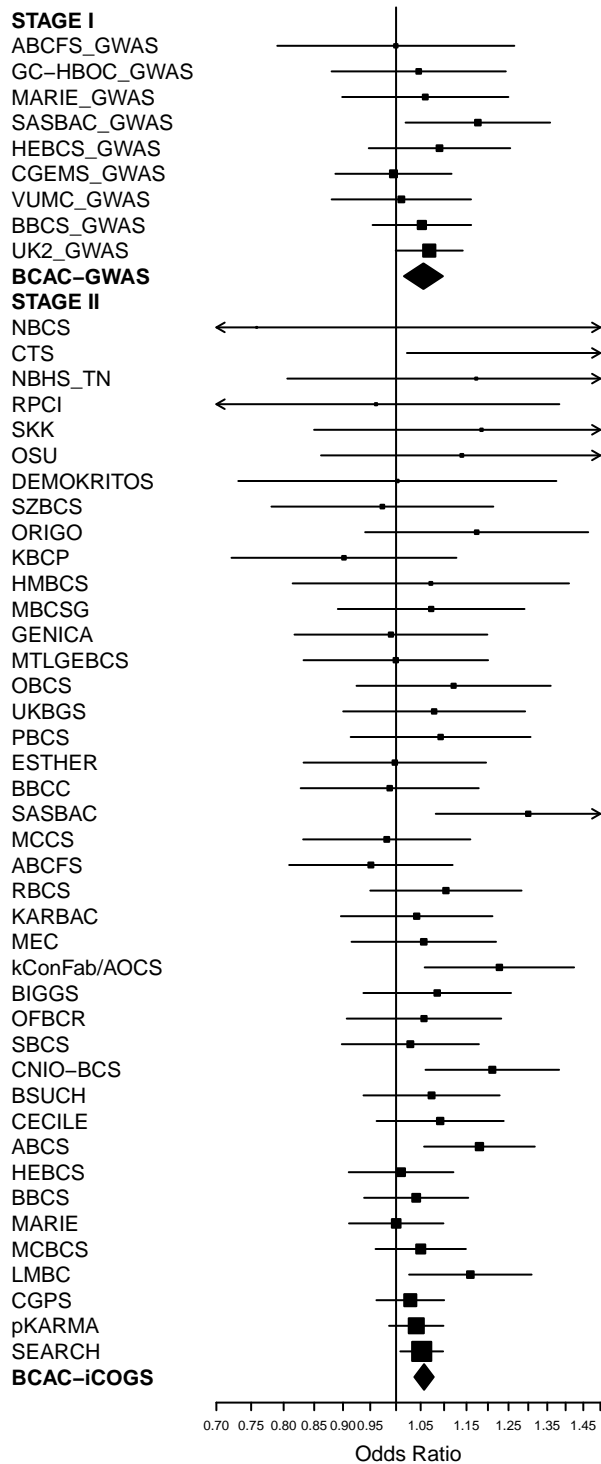
NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.33  
I<sup>2</sup> iCOGS=7.97







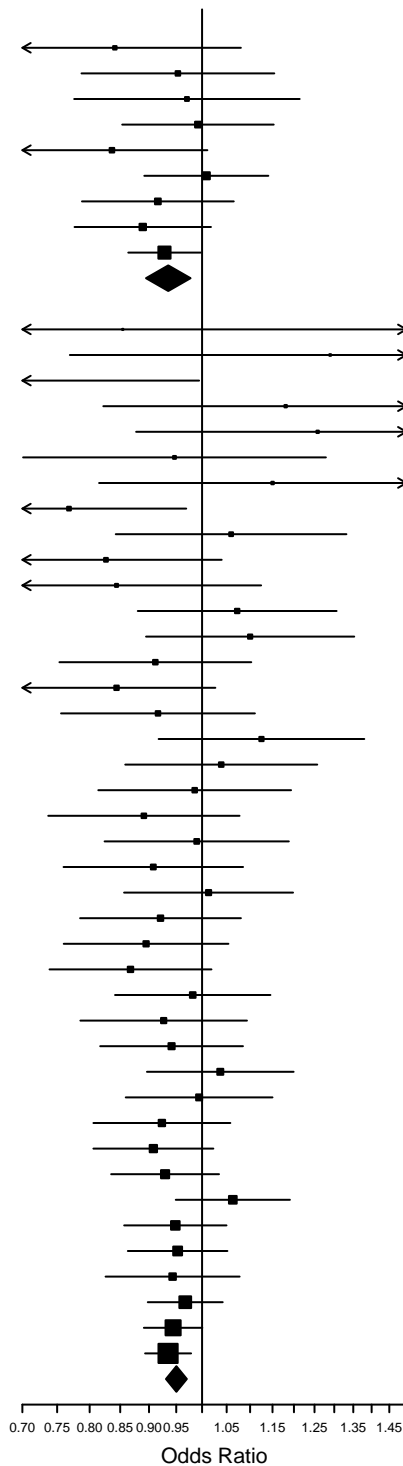
p-het iCOGS=0.57  
I^2 iCOGS=0

**STAGE I**

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**

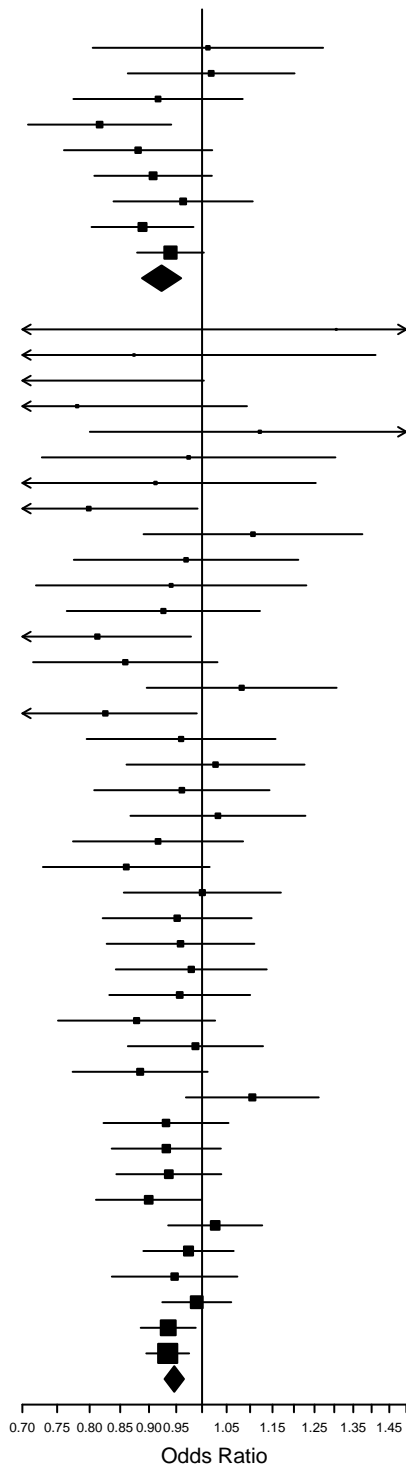


**STAGE I**

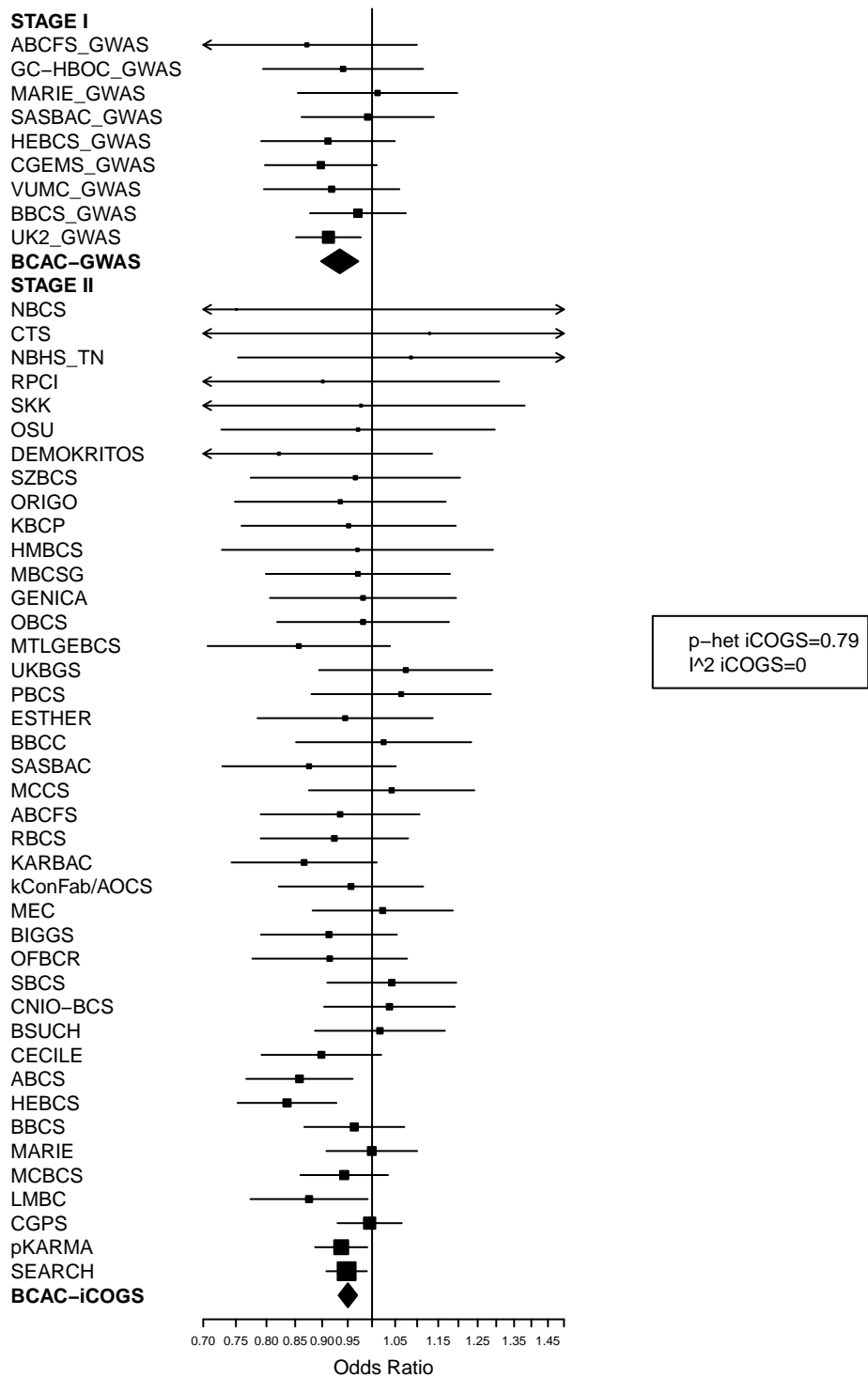
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
MEC  
kConFab/AOCS  
BIGGS  
OFBCR  
SBSCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.65  
I<sup>2</sup> iCOGS=0

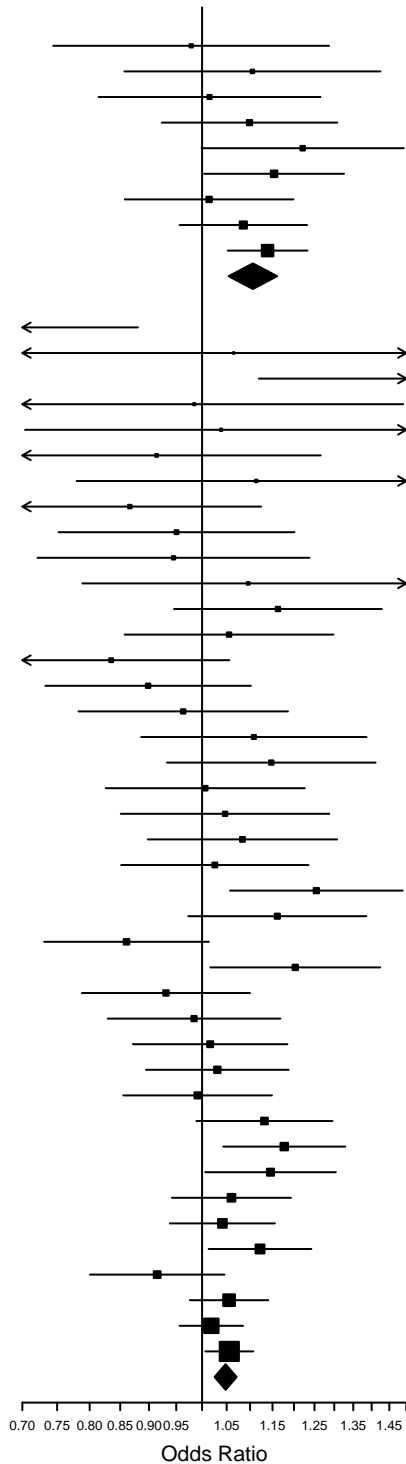


**STAGE I**

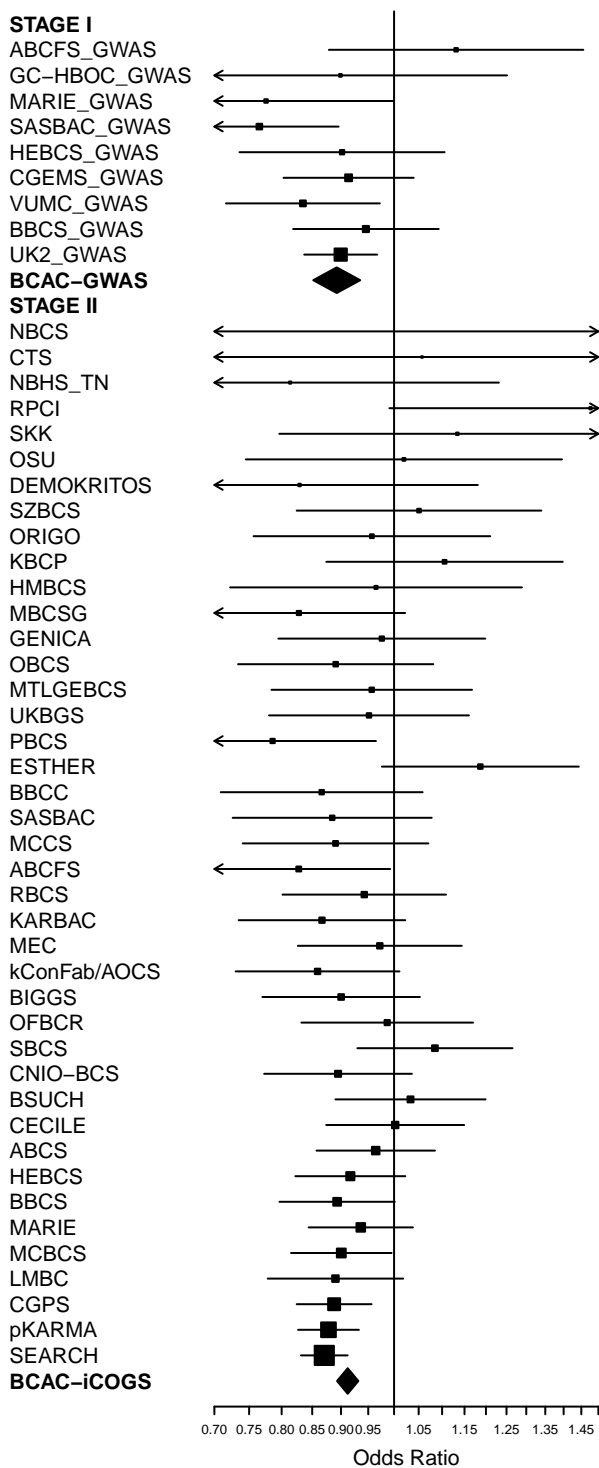
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

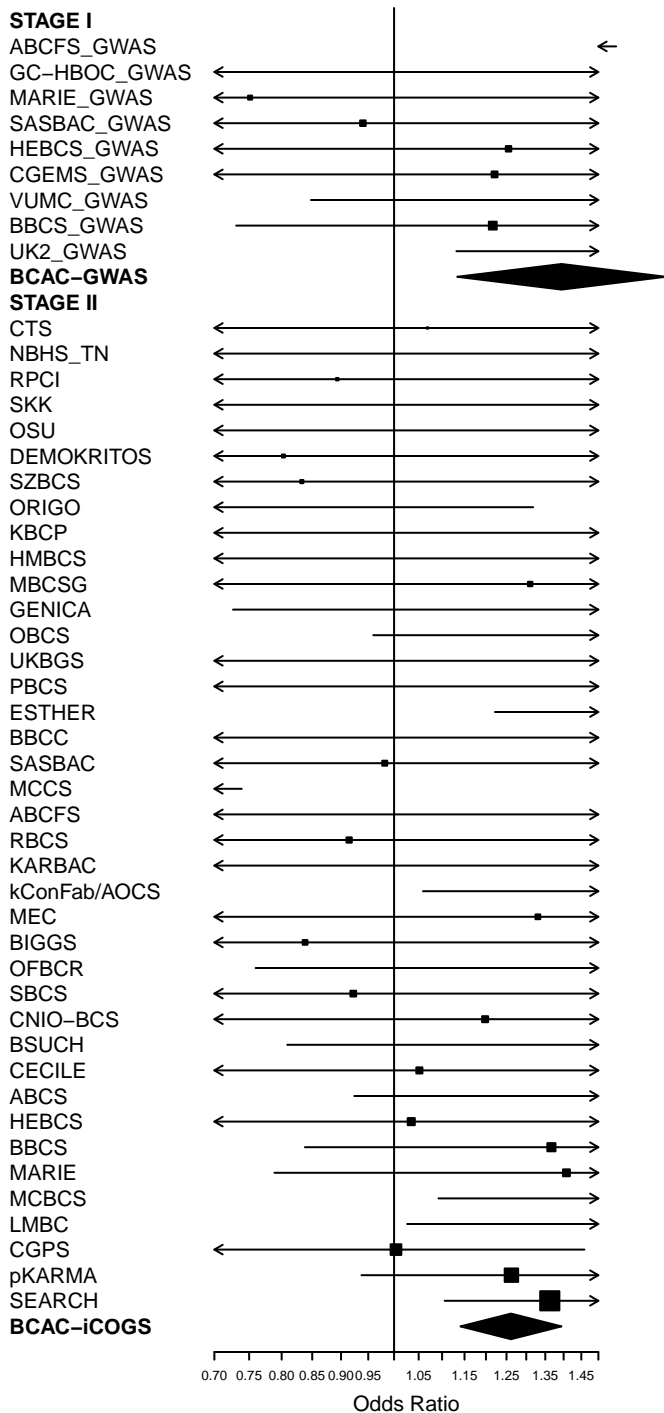
**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
MEC  
kConFab/AOCS  
BIGGS  
OFBCR  
SBSCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**

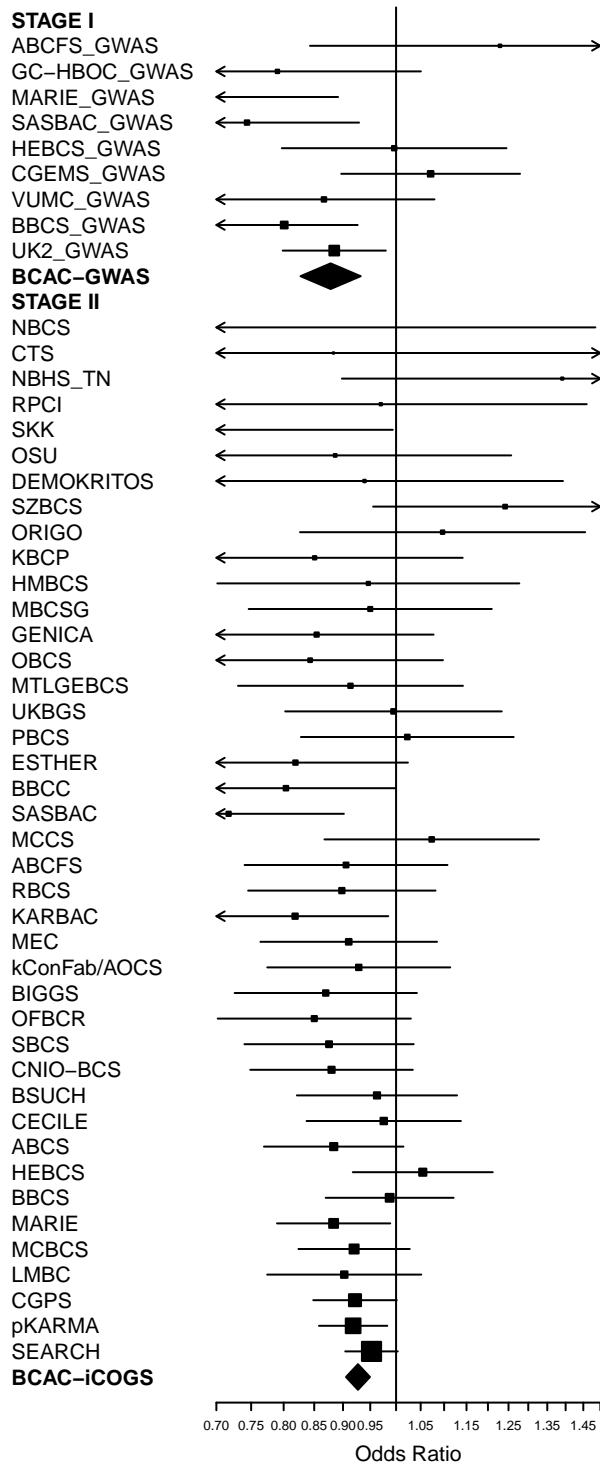


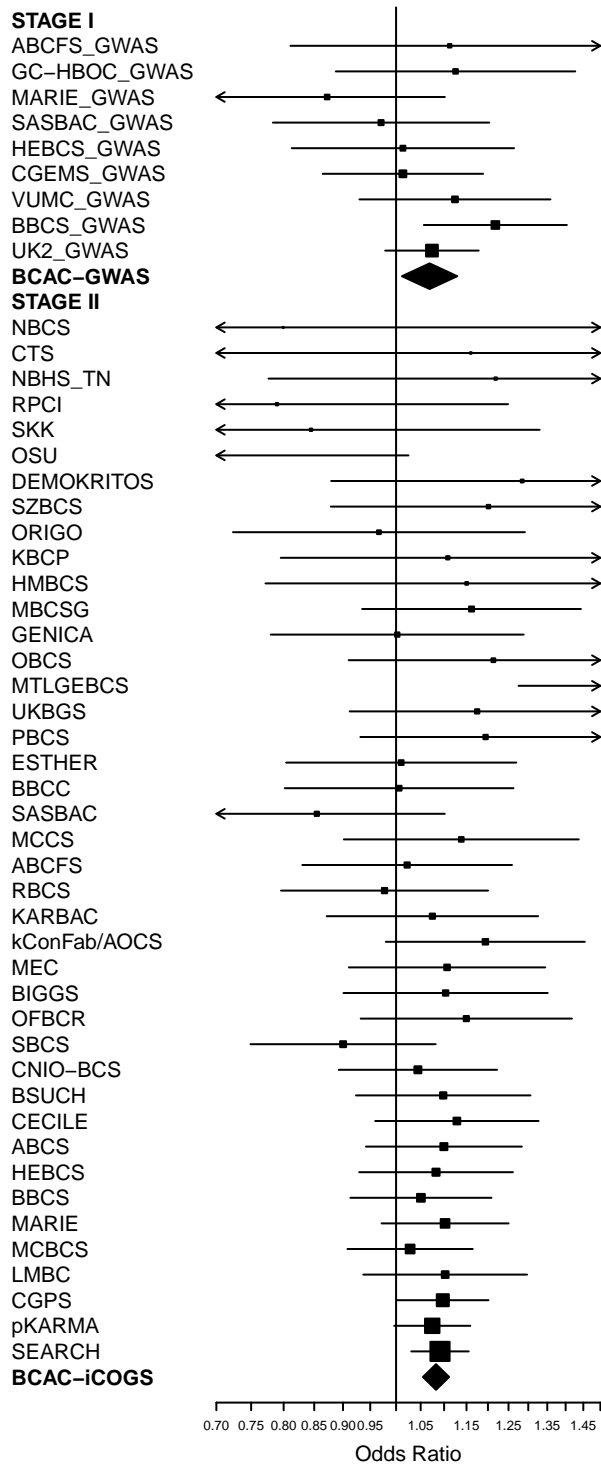
p-het iCOGS=0.06  
 $I^2$  iCOGS=27.4

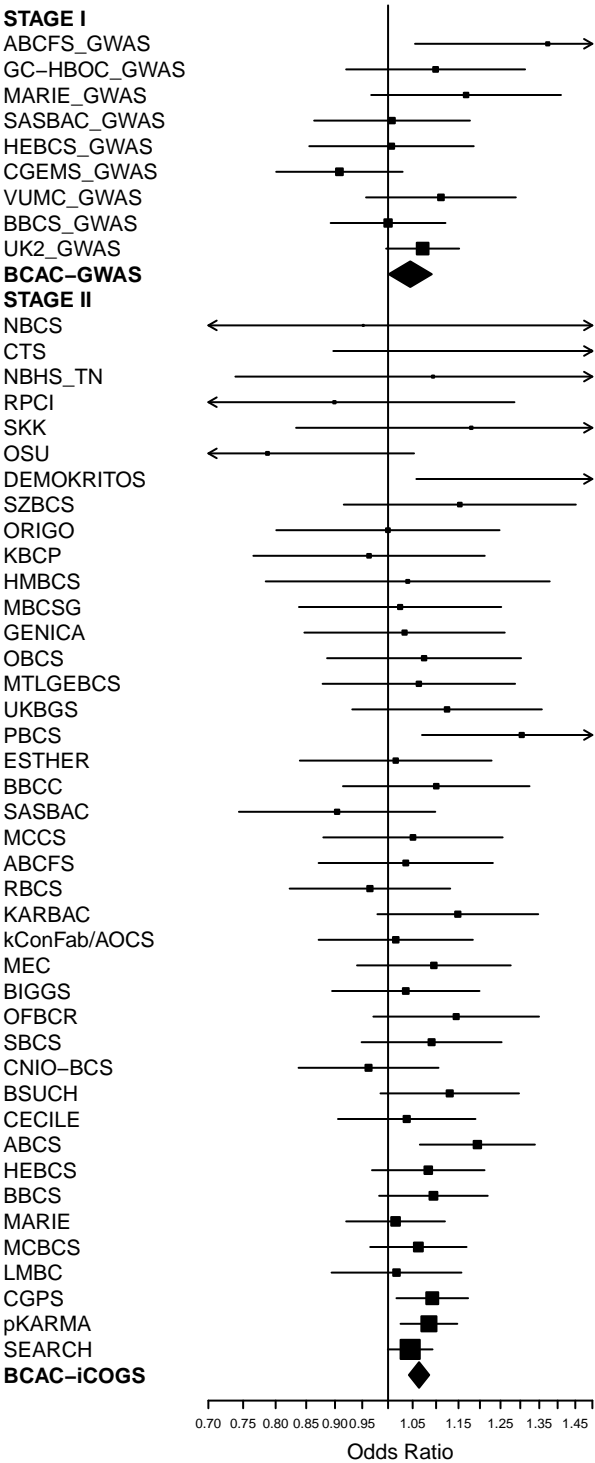


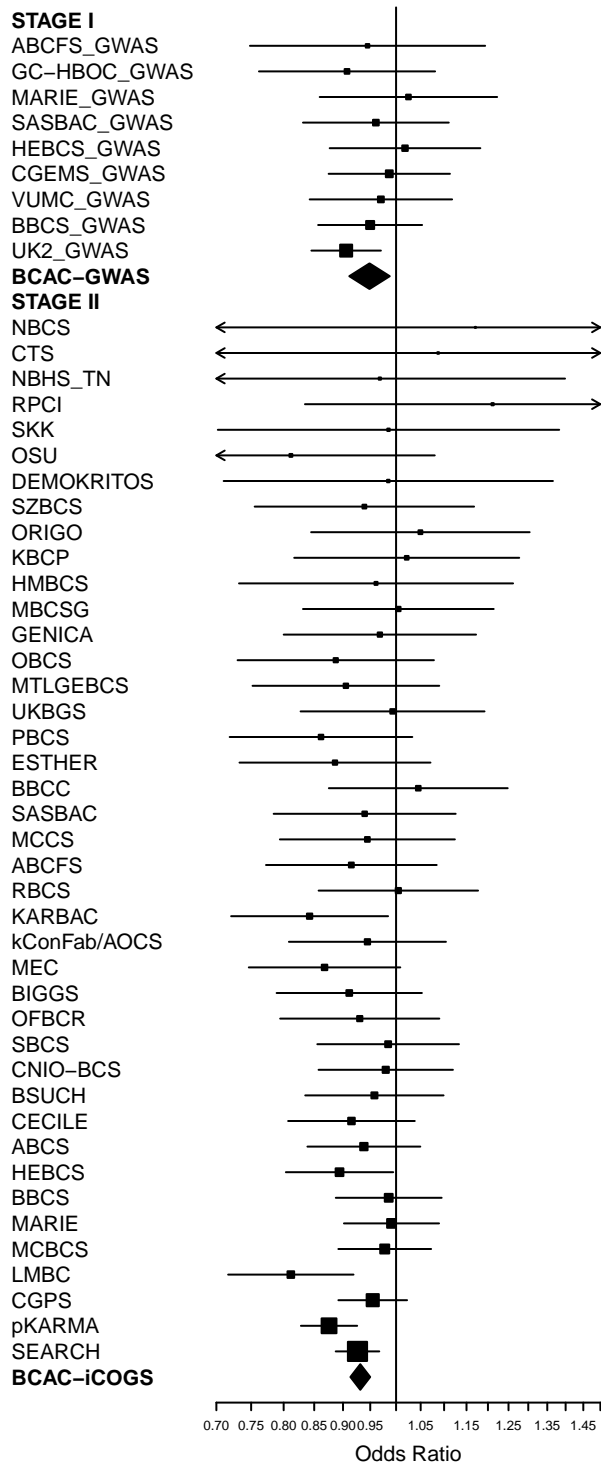




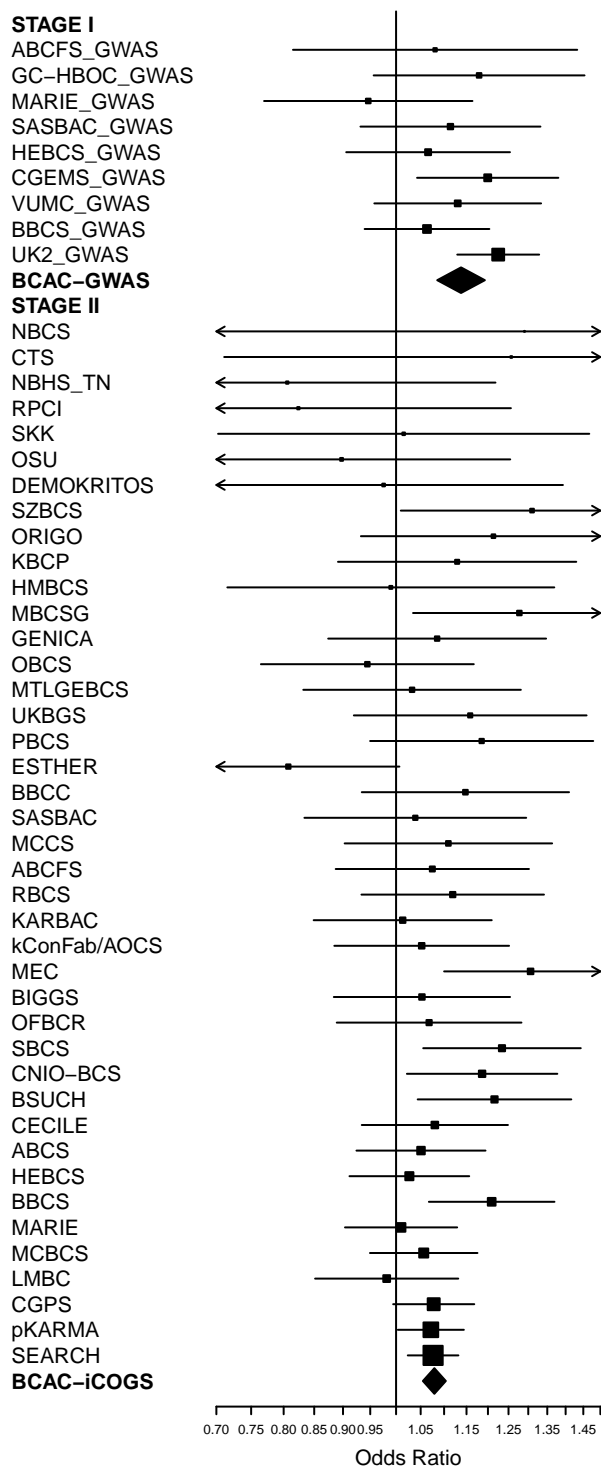








p-het iCOGS=0.87  
I<sup>2</sup> iCOGS=0



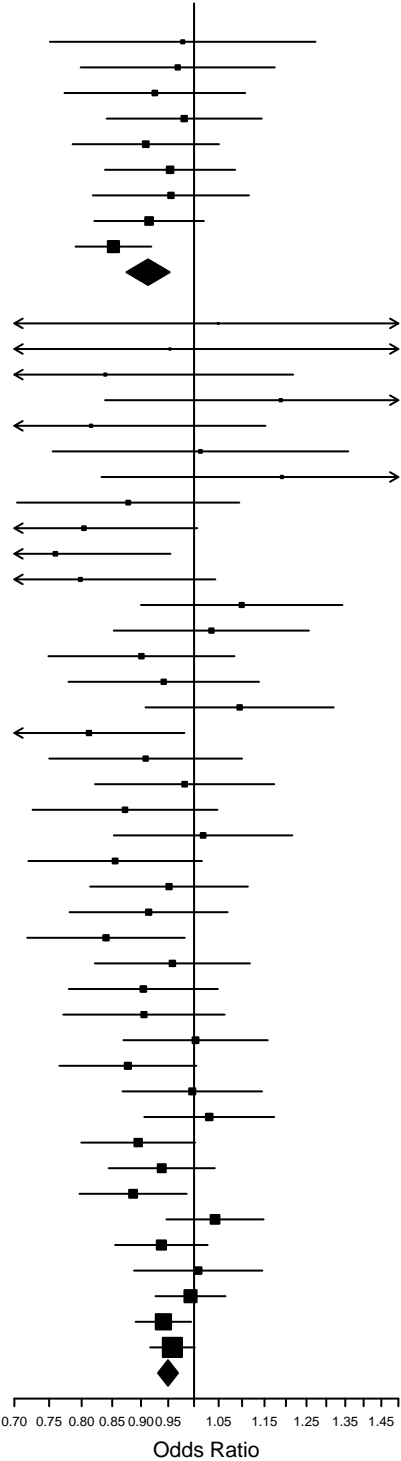
STAGE I

ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

BCAC-GWAS

STAGE II

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
BCAC-iCOGS



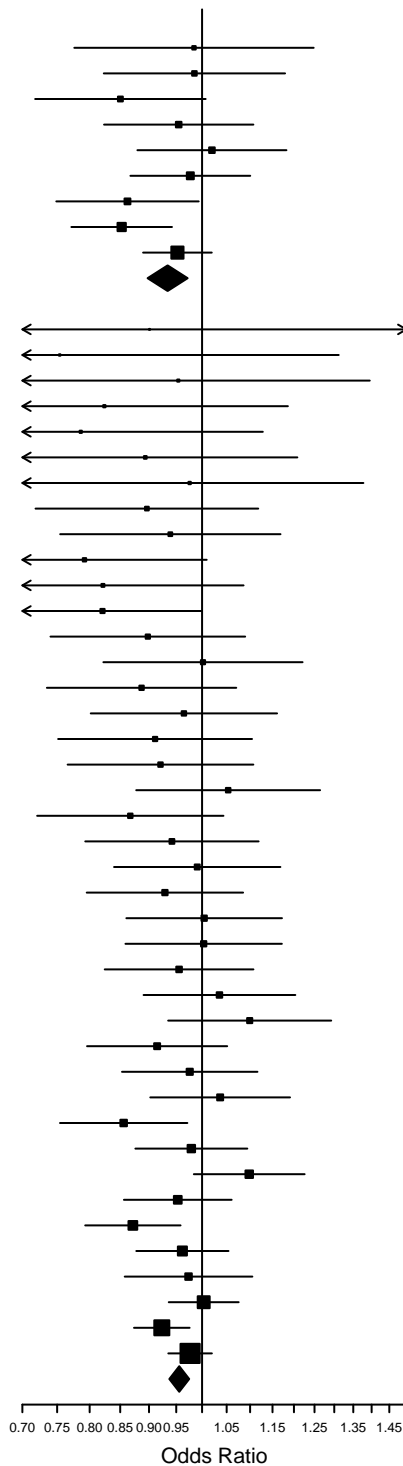
p-het iCOGS=0.56  
I<sup>2</sup> iCOGS=0

**STAGE I**

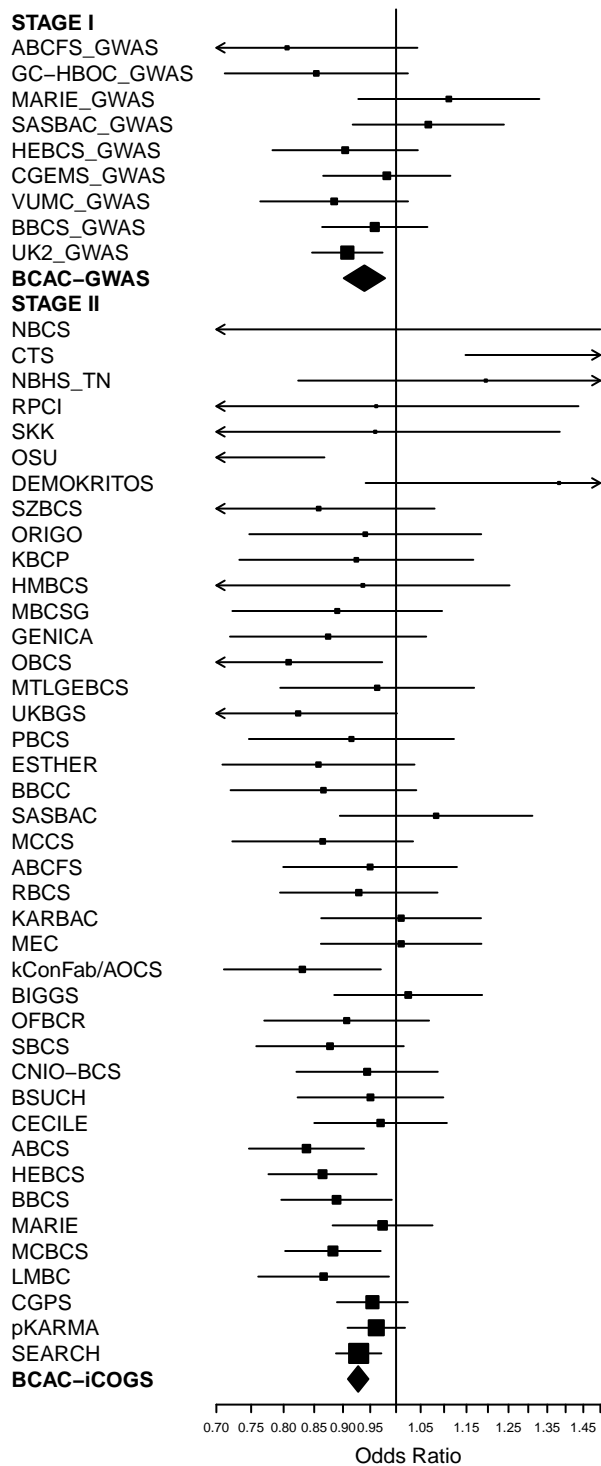
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
MBCSG  
GENICA  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
kConFab/AOCS  
MEC  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**



p-het iCOGS=0.58  
 $I^2$  iCOGS=0



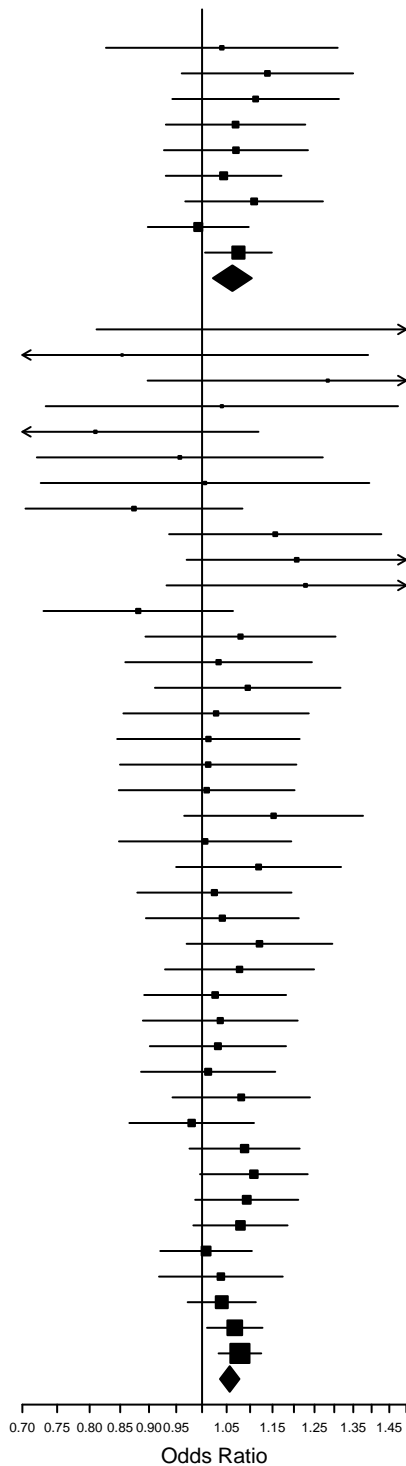


**STAGE I**

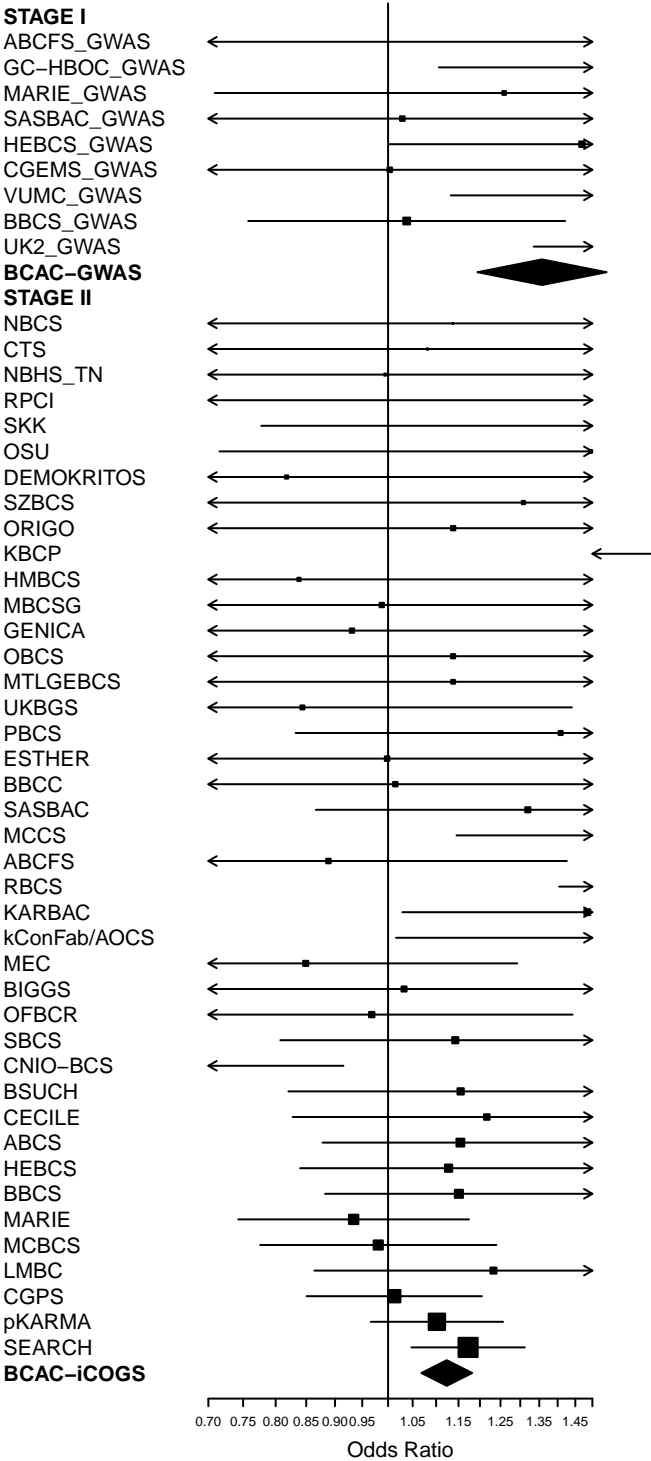
ABCFS\_GWAS  
GC-HBOC\_GWAS  
MARIE\_GWAS  
SASBAC\_GWAS  
HEBCS\_GWAS  
CGEMS\_GWAS  
VUMC\_GWAS  
BBCS\_GWAS  
UK2\_GWAS

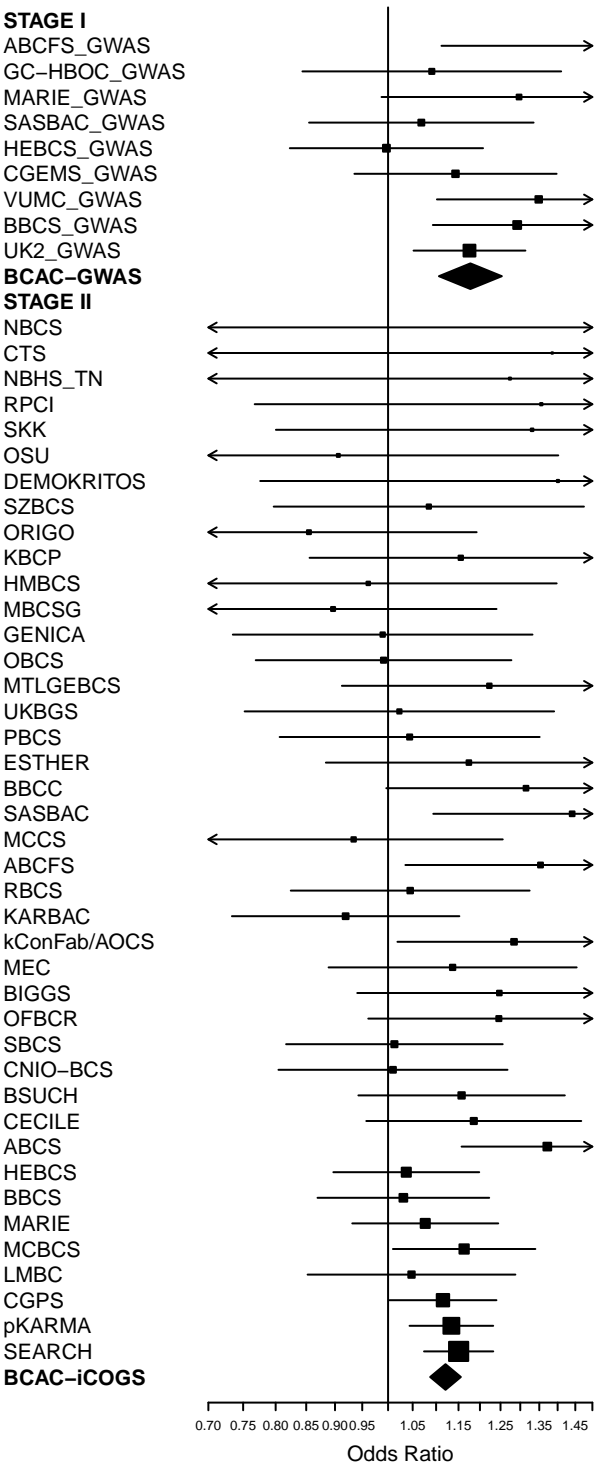
**BCAC-GWAS****STAGE II**

NBCS  
CTS  
NBHS\_TN  
RPCI  
SKK  
OSU  
DEMOKRITOS  
SZBCS  
ORIGO  
KBCP  
HMBCS  
GENICA  
MBCSG  
OBCS  
MTLGEBCS  
UKBGS  
PBCS  
ESTHER  
BBCC  
SASBAC  
MCCS  
ABCFS  
RBCS  
KARBAC  
MEC  
kConFab/AOCS  
BIGGS  
OFBCR  
SBCS  
CNIO-BCS  
BSUCH  
CECILE  
ABCS  
HEBCS  
BBCS  
MARIE  
MCBCS  
LMBC  
CGPS  
pKARMA  
SEARCH  
**BCAC-iCOGS**

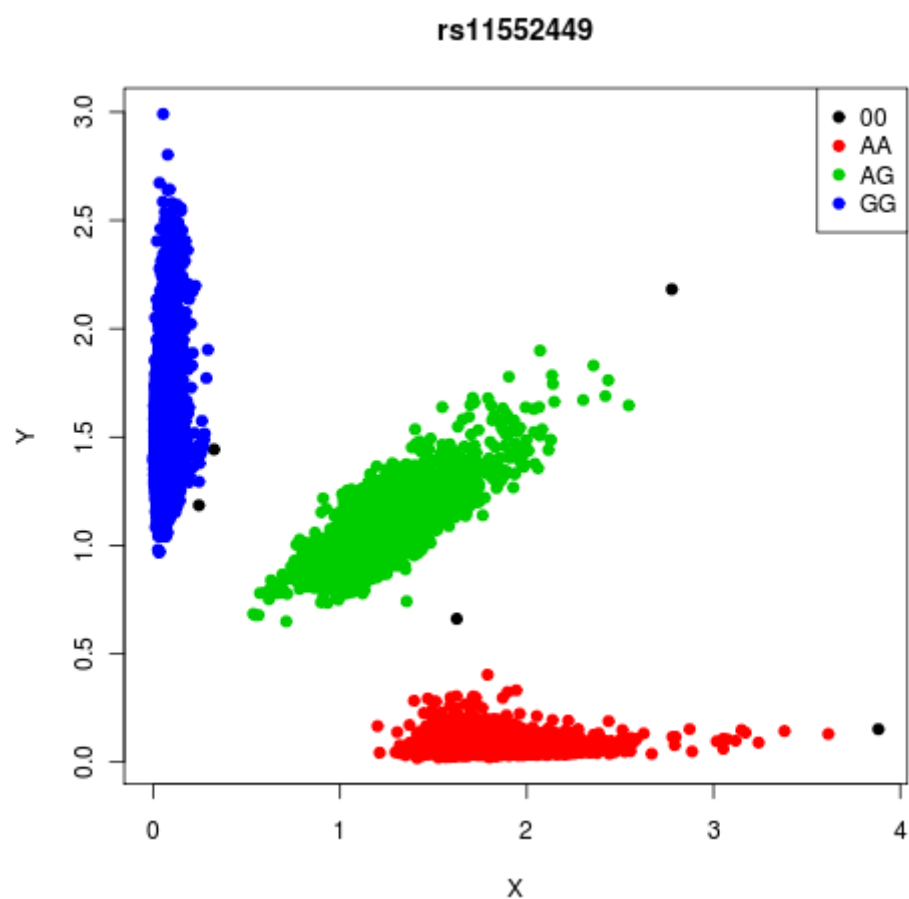
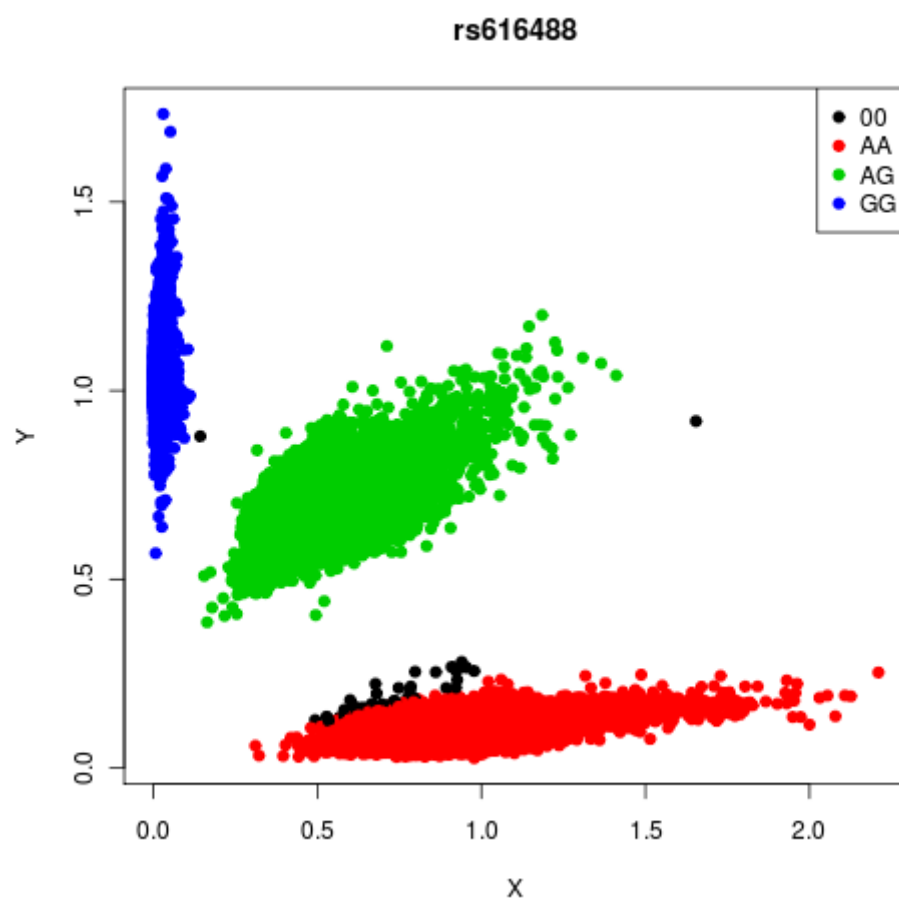


p-het iCOGS=0.94  
 $I^2$  iCOGS=0

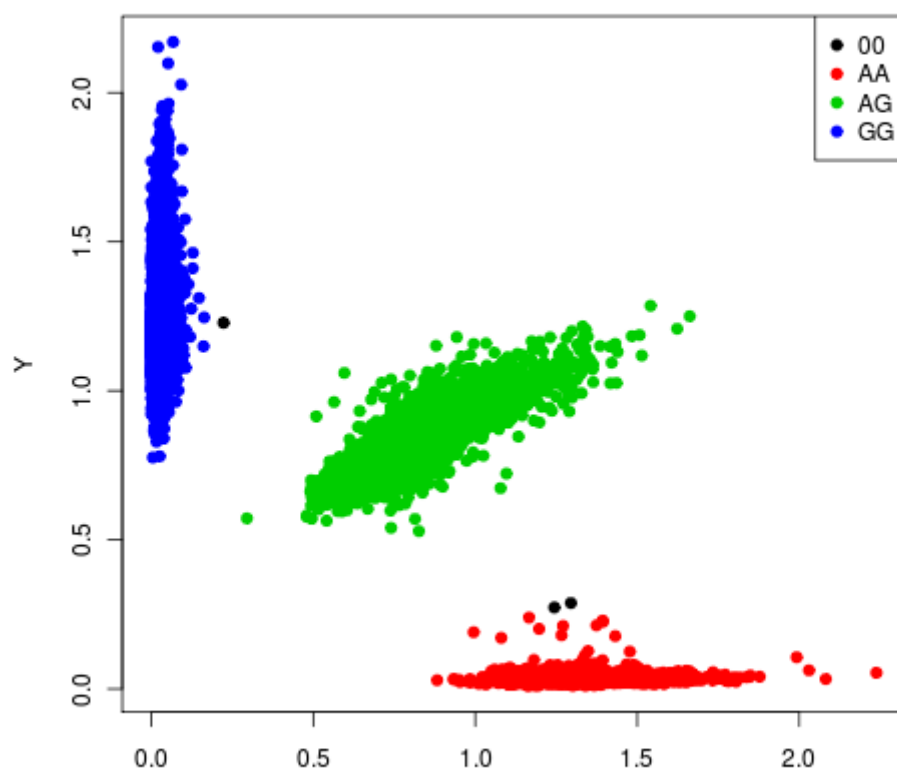




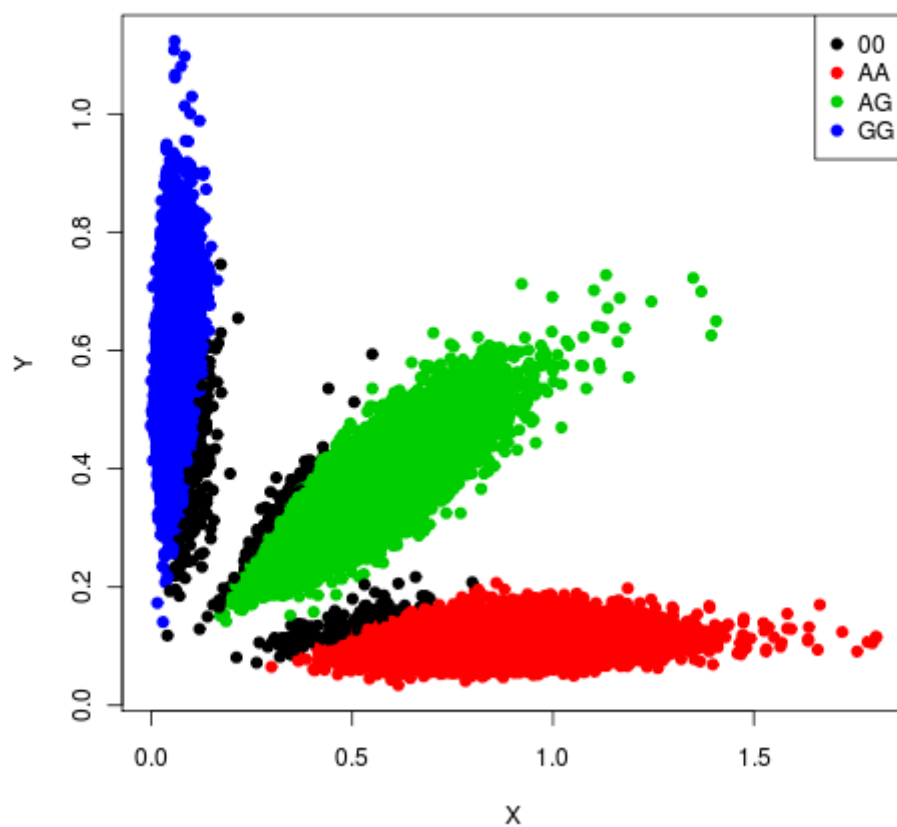
**Supplementary Figure 3.** Cluster plots for the normalised intensities of the two alleles, over all BCAC studies, for 41 SNPs achieving genome-wide significance.

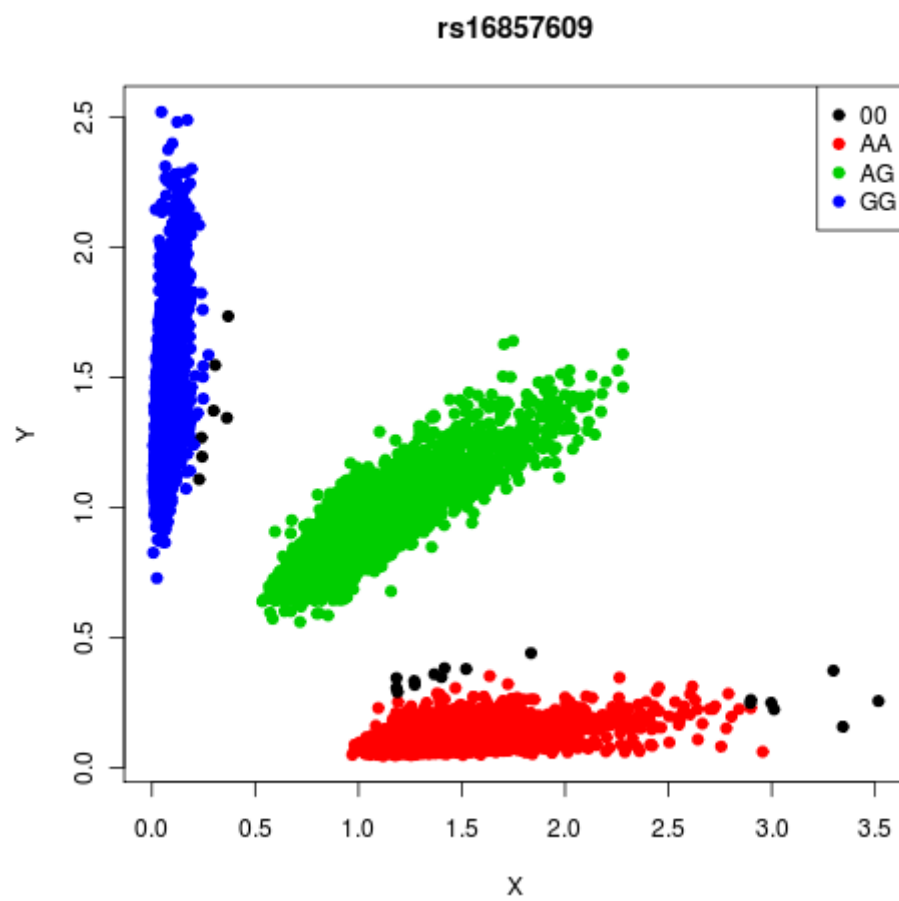
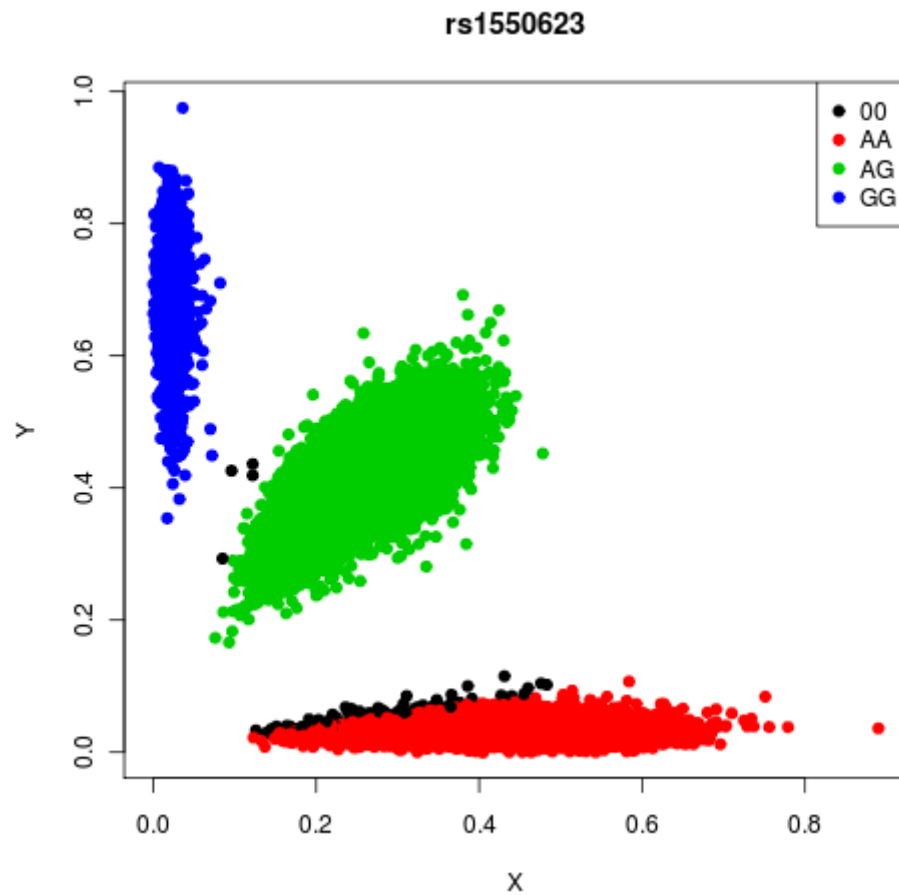


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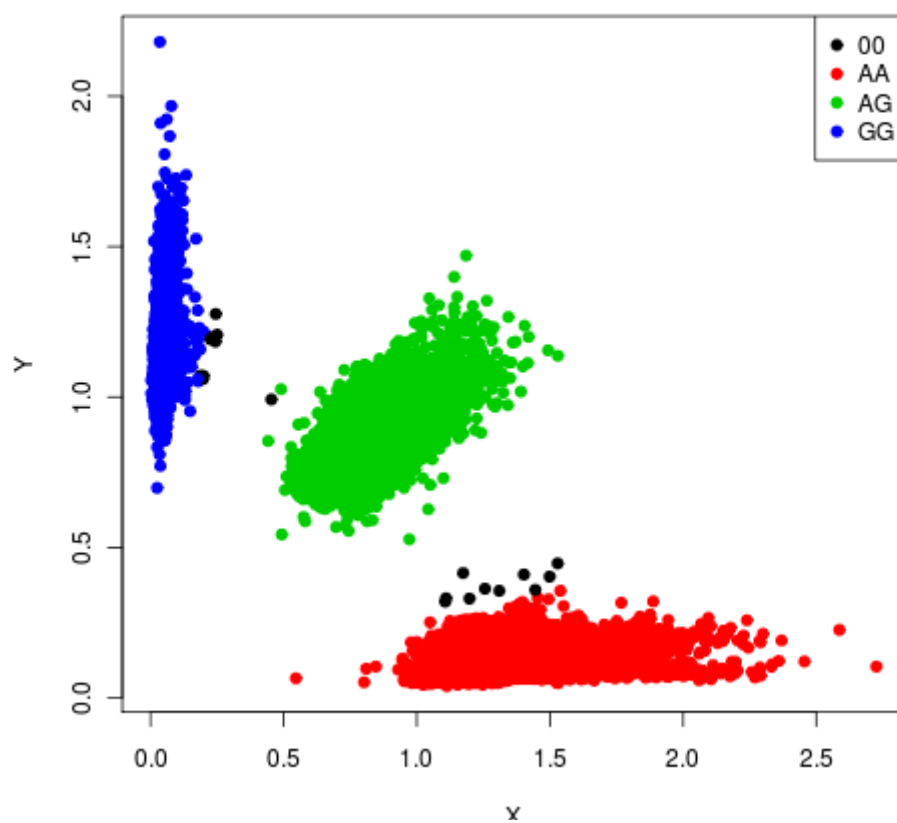


rs2016394

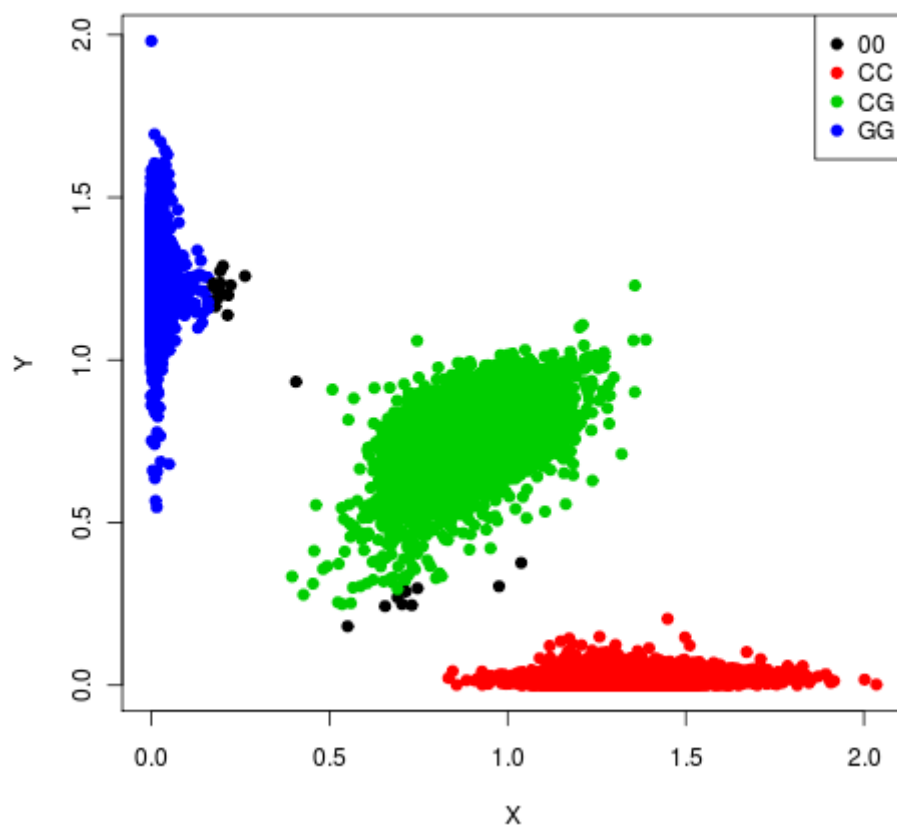




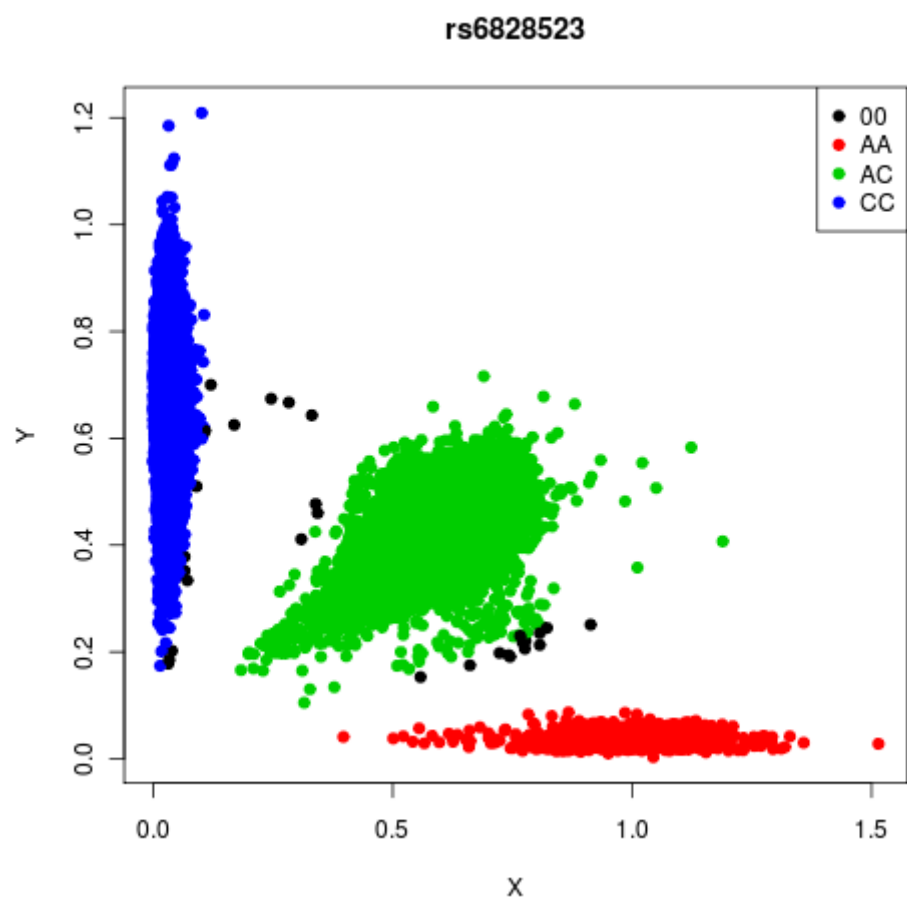
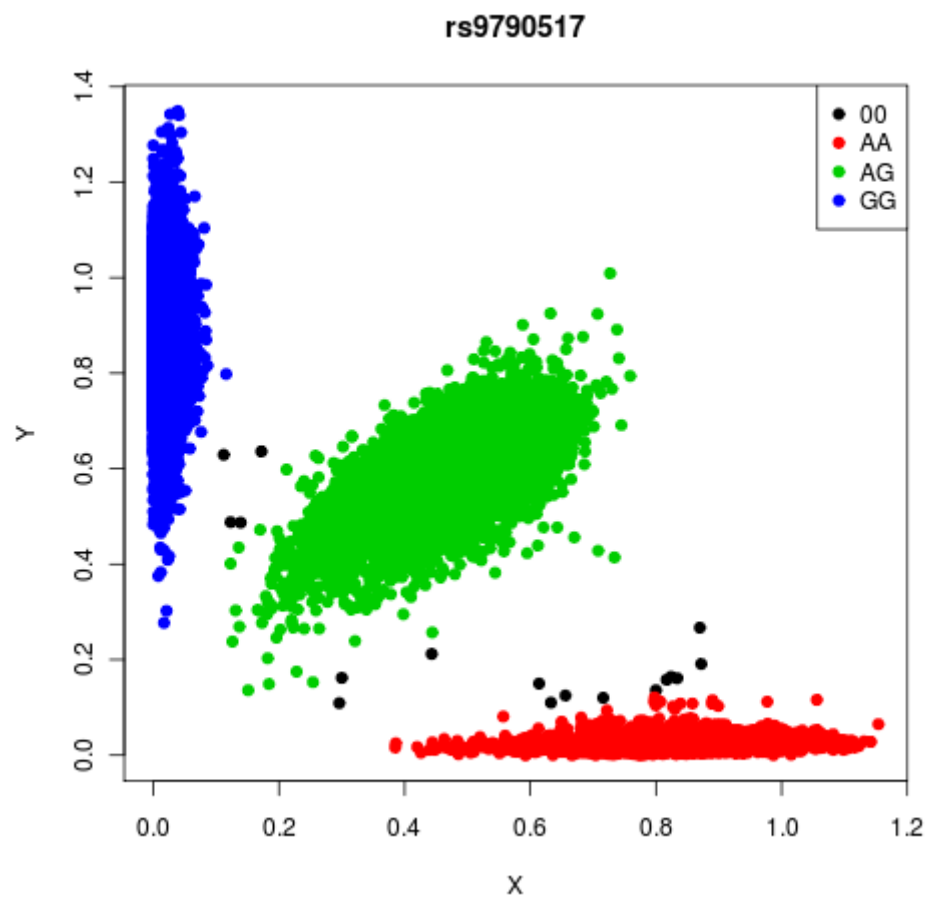
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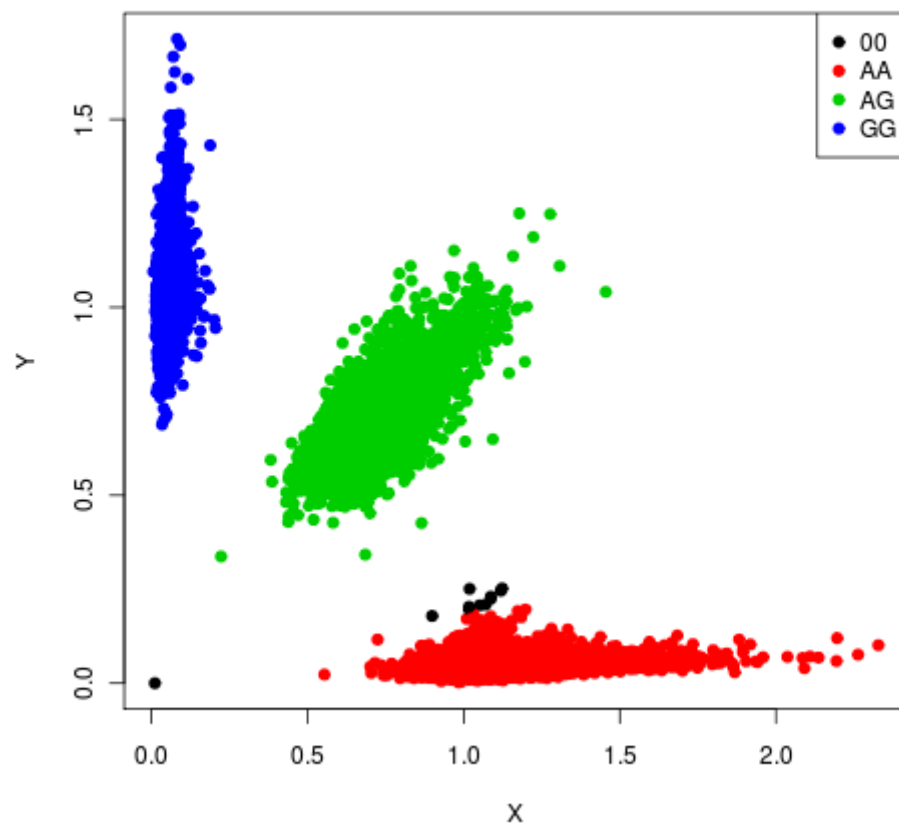
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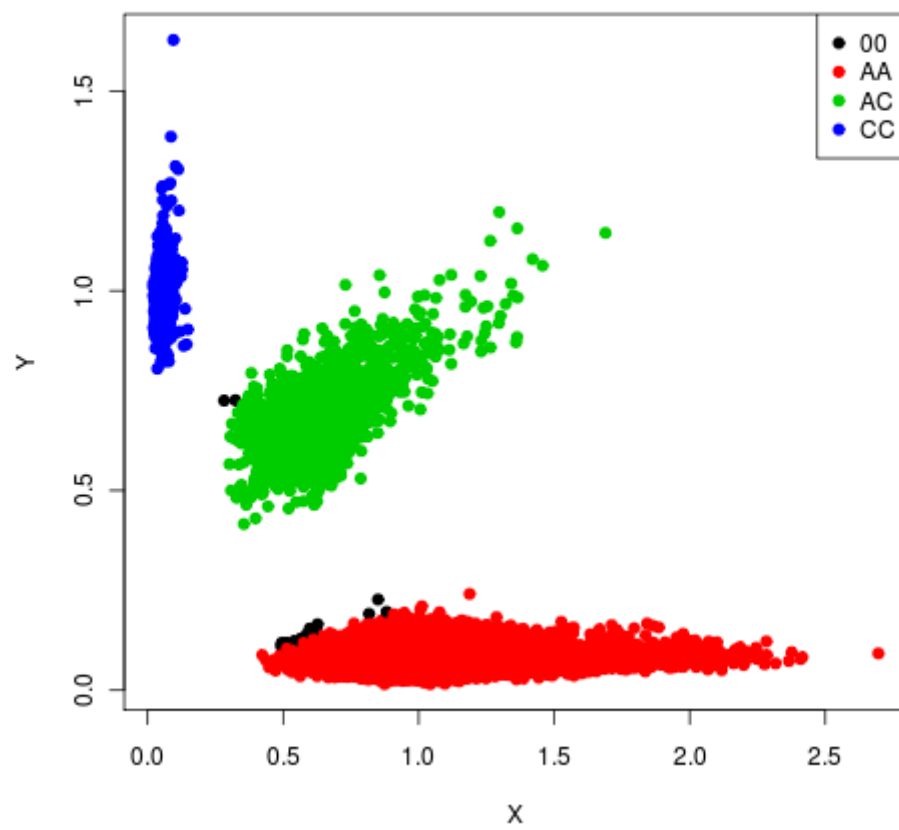


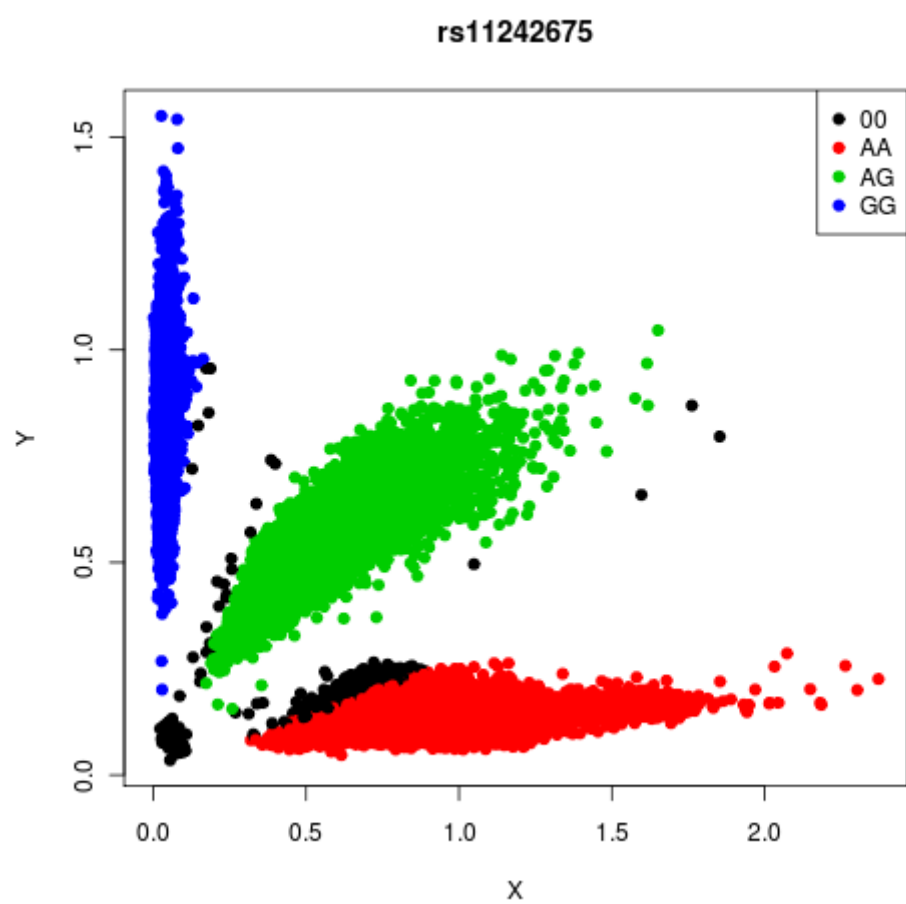
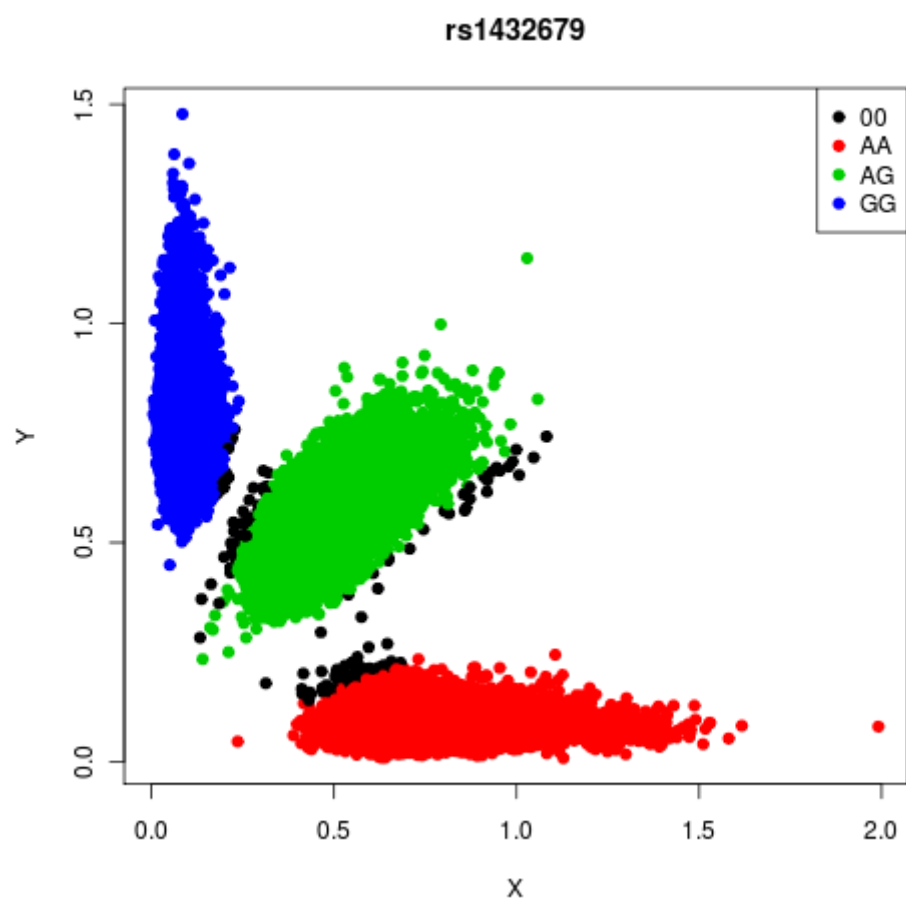


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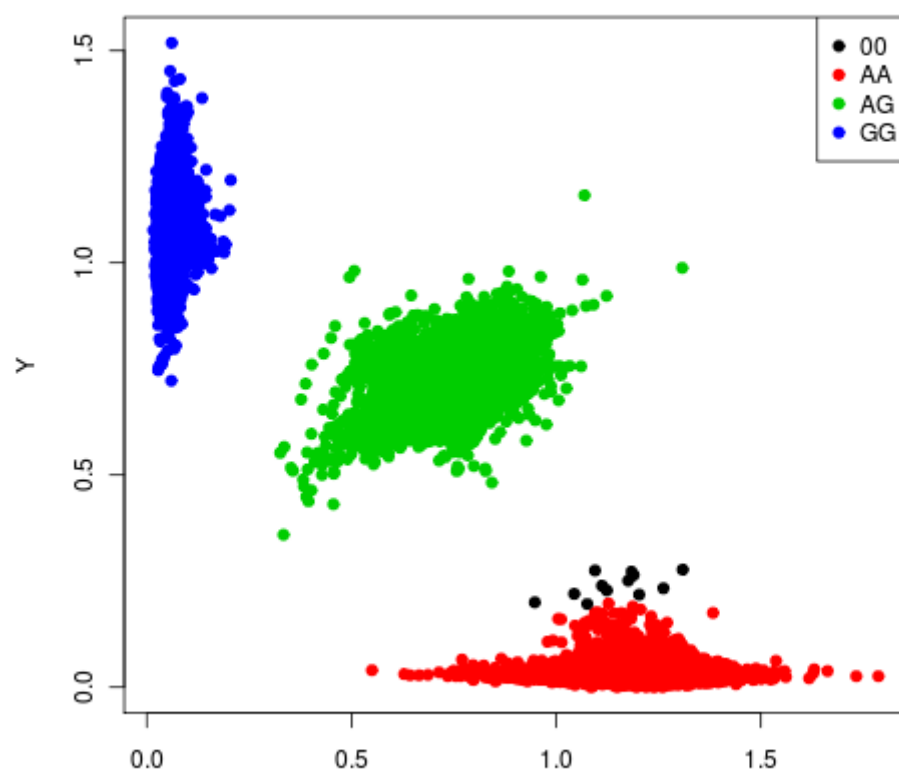


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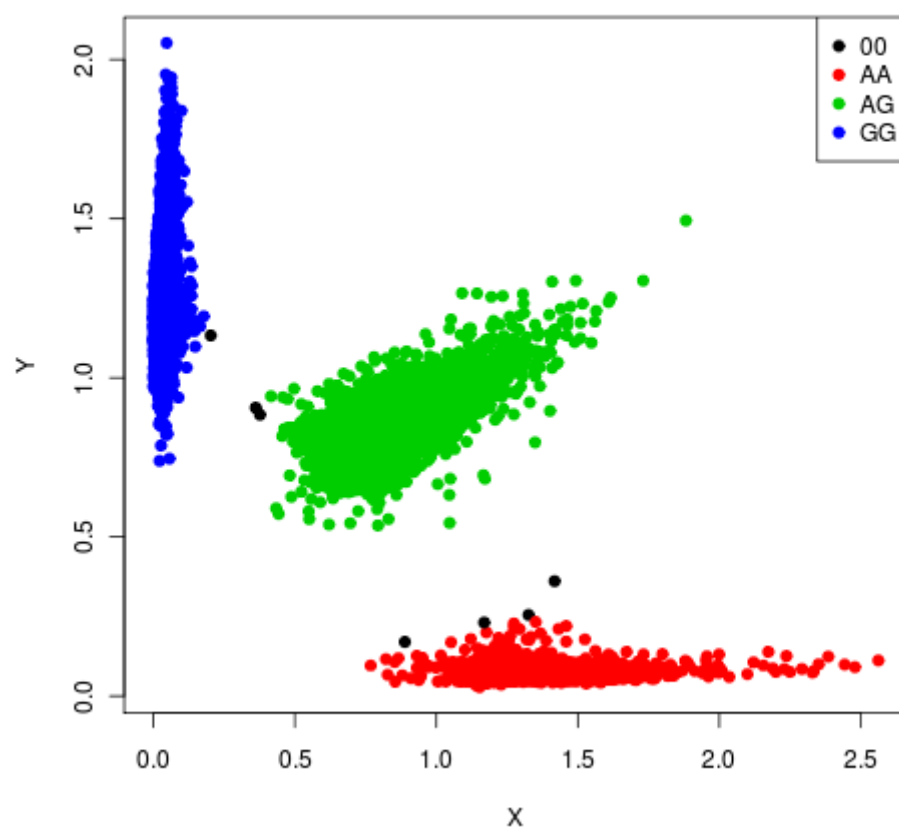




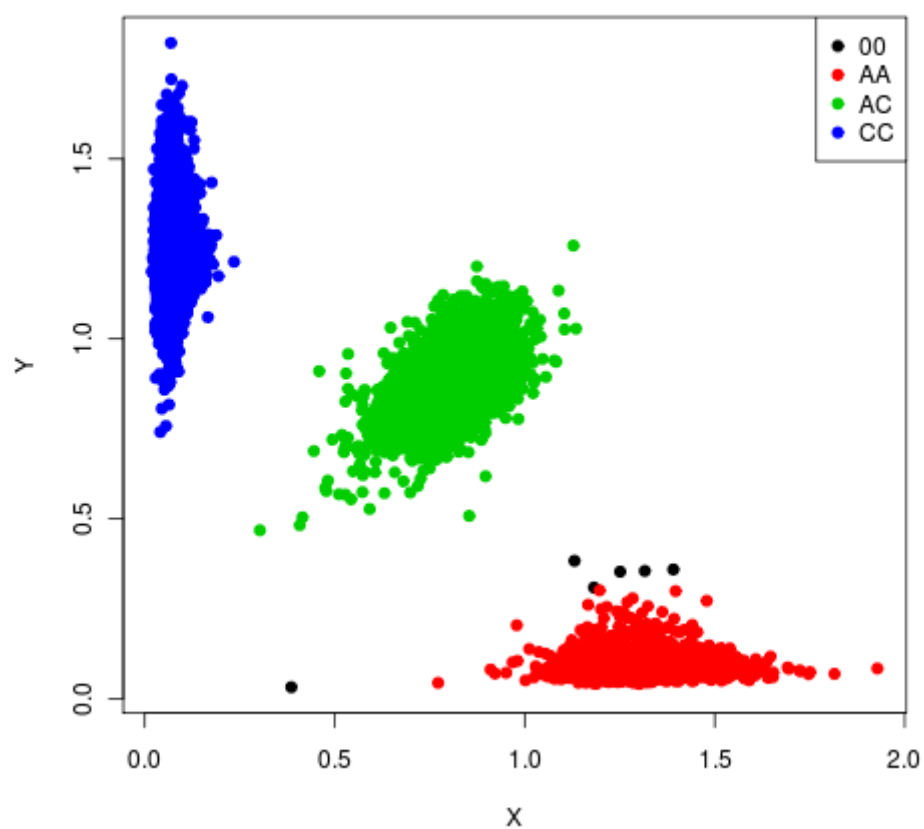
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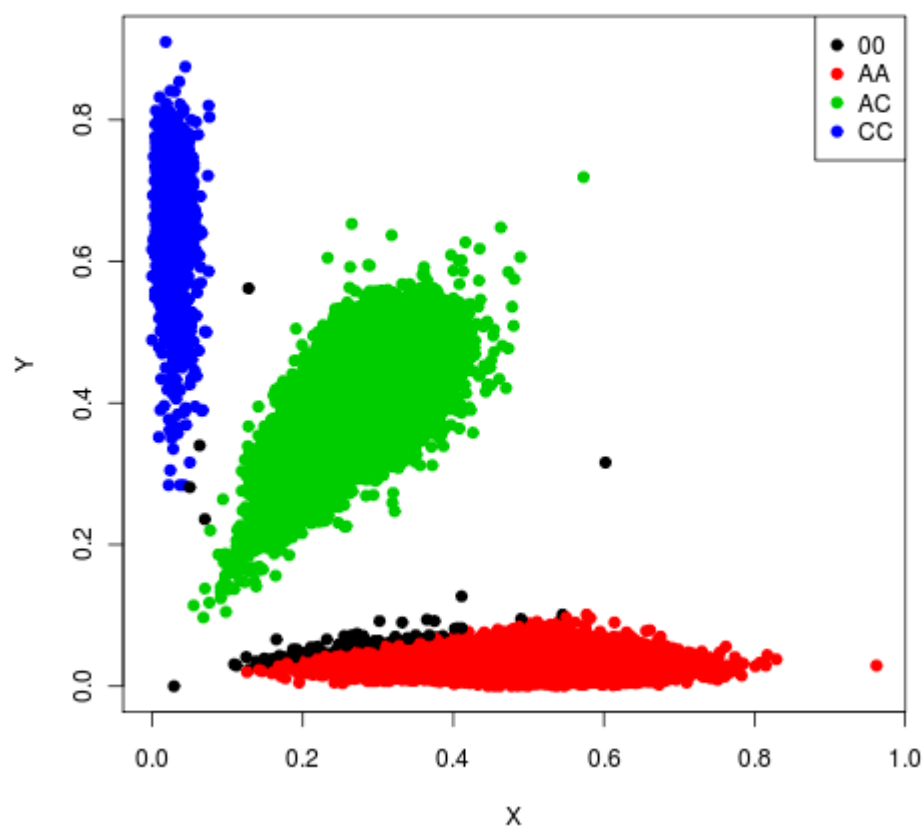
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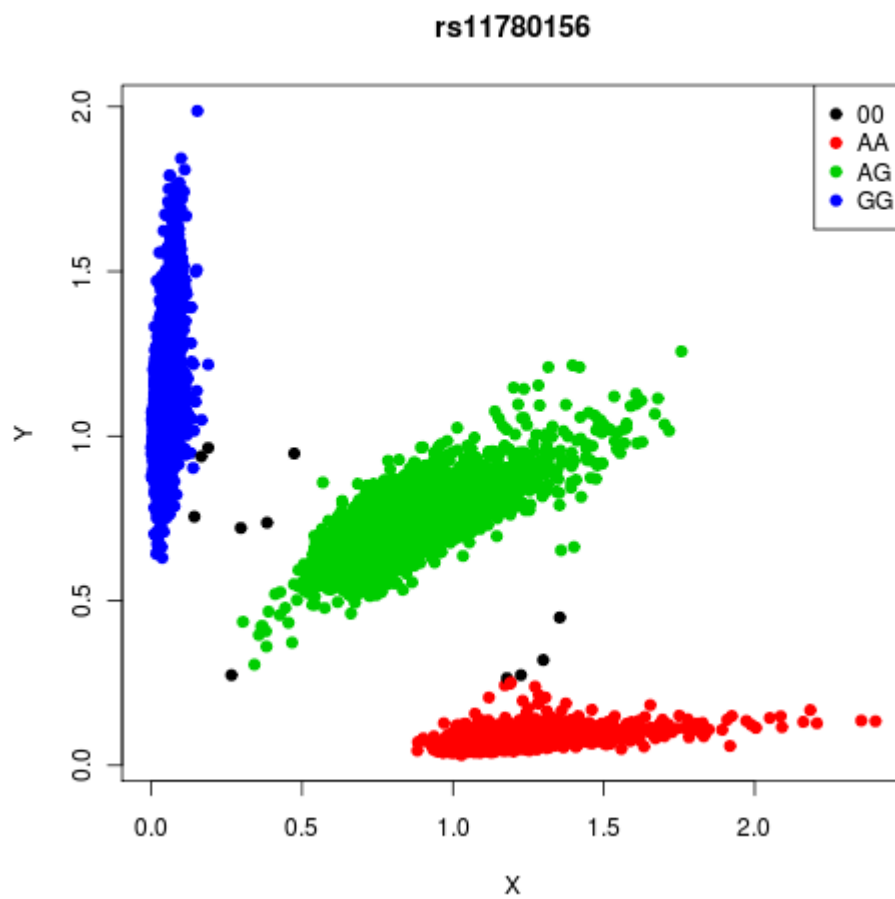
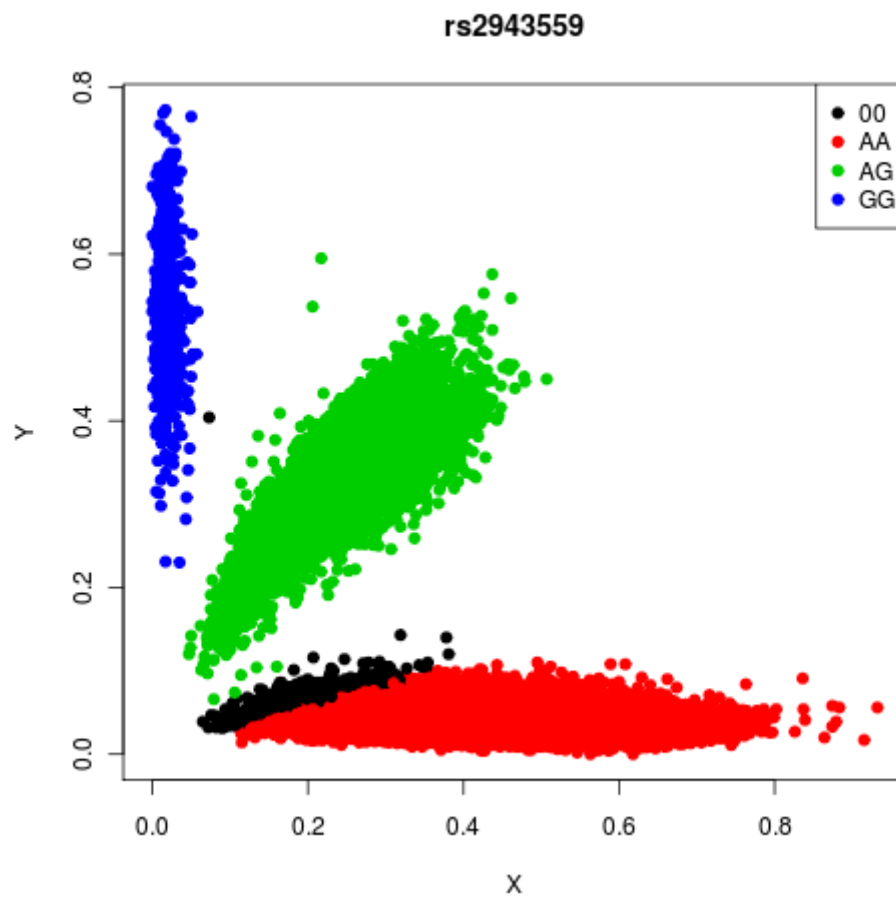


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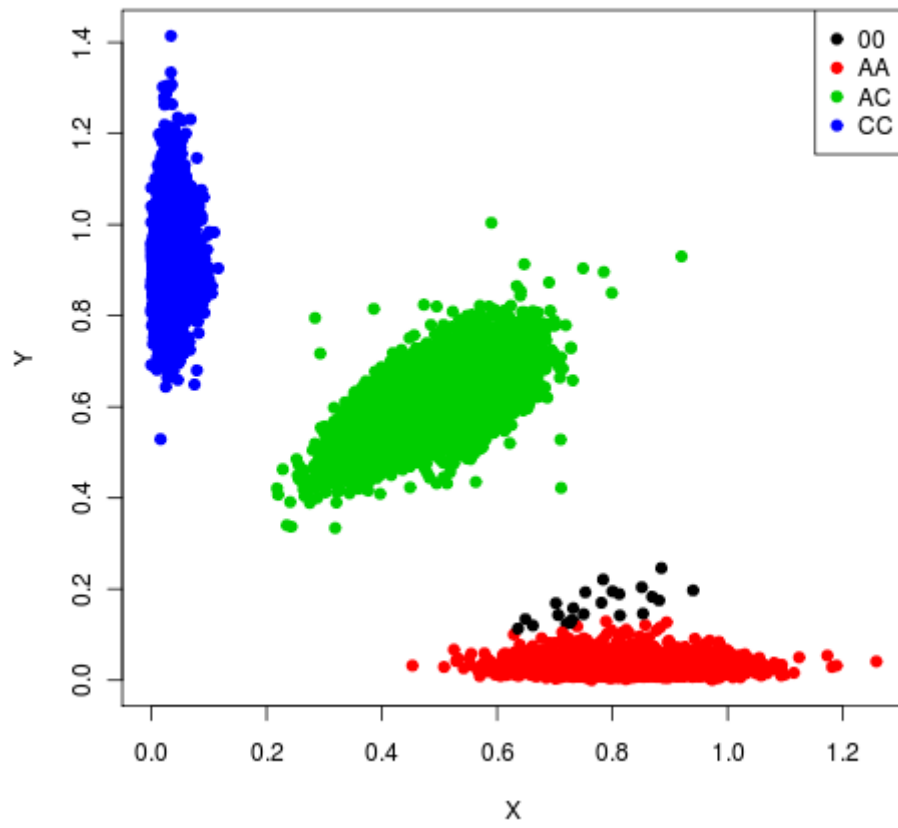


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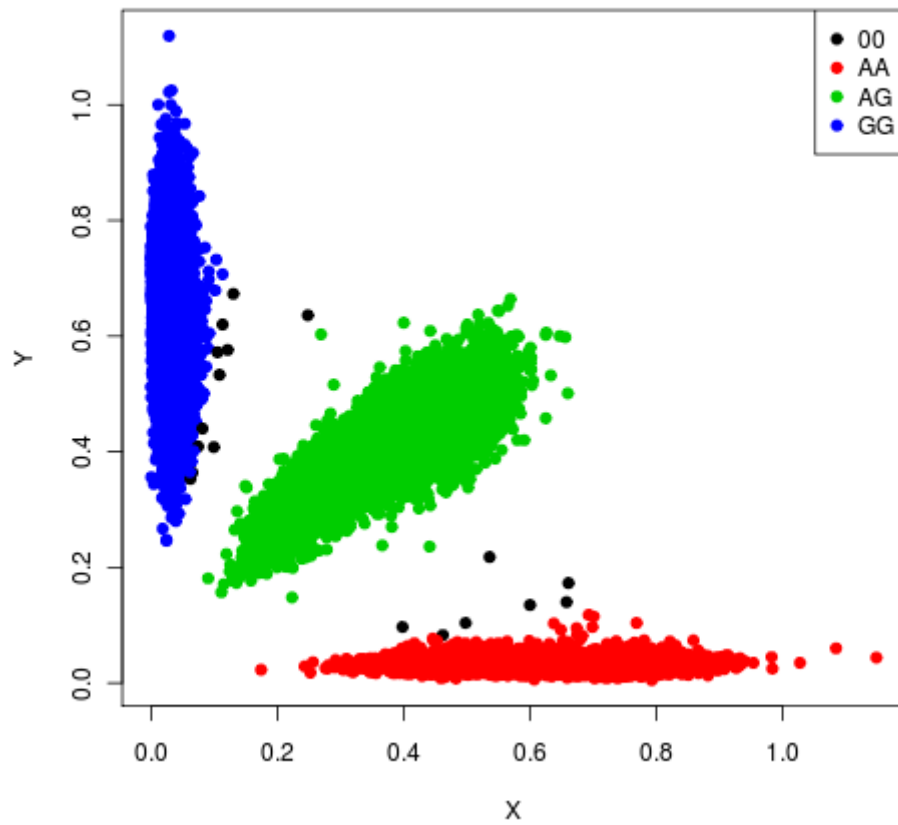




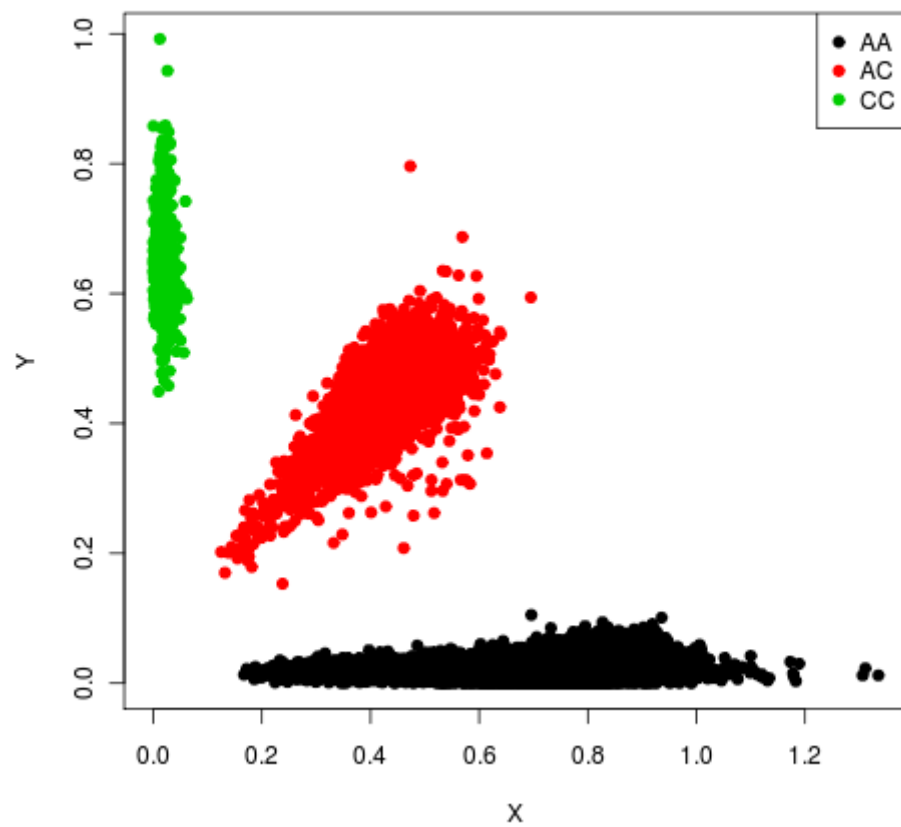
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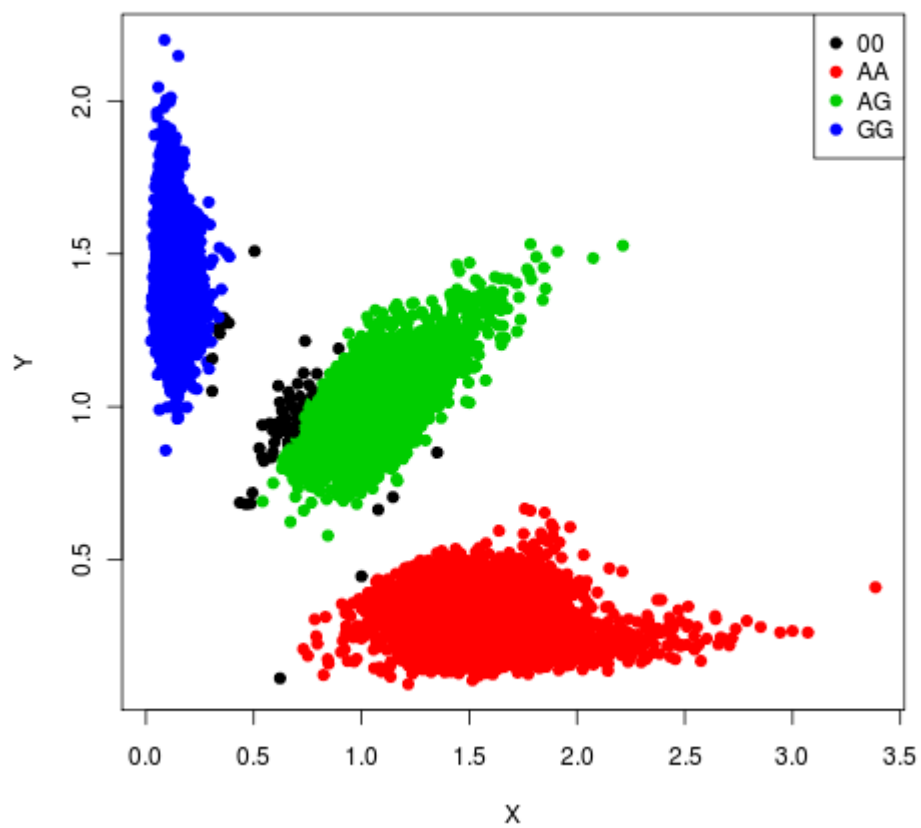
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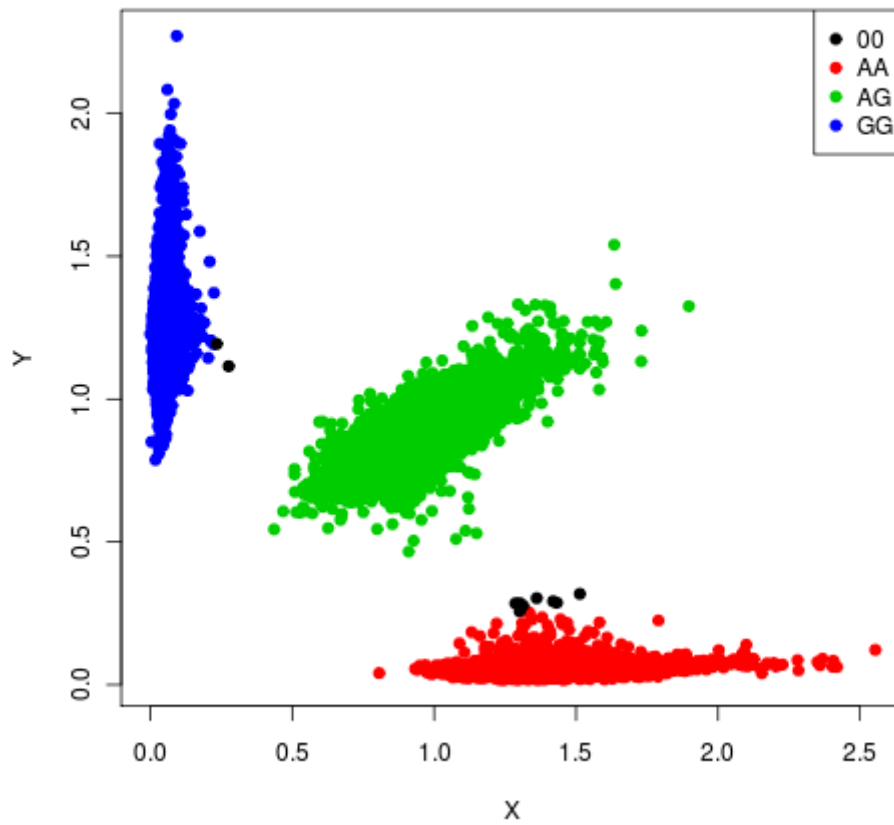


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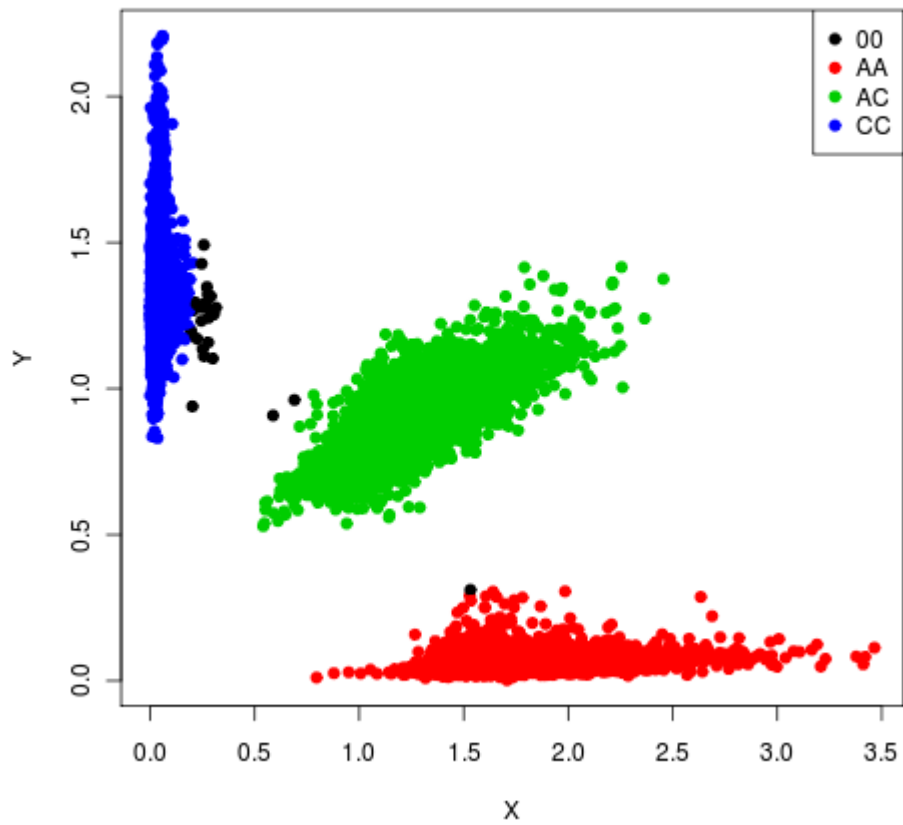


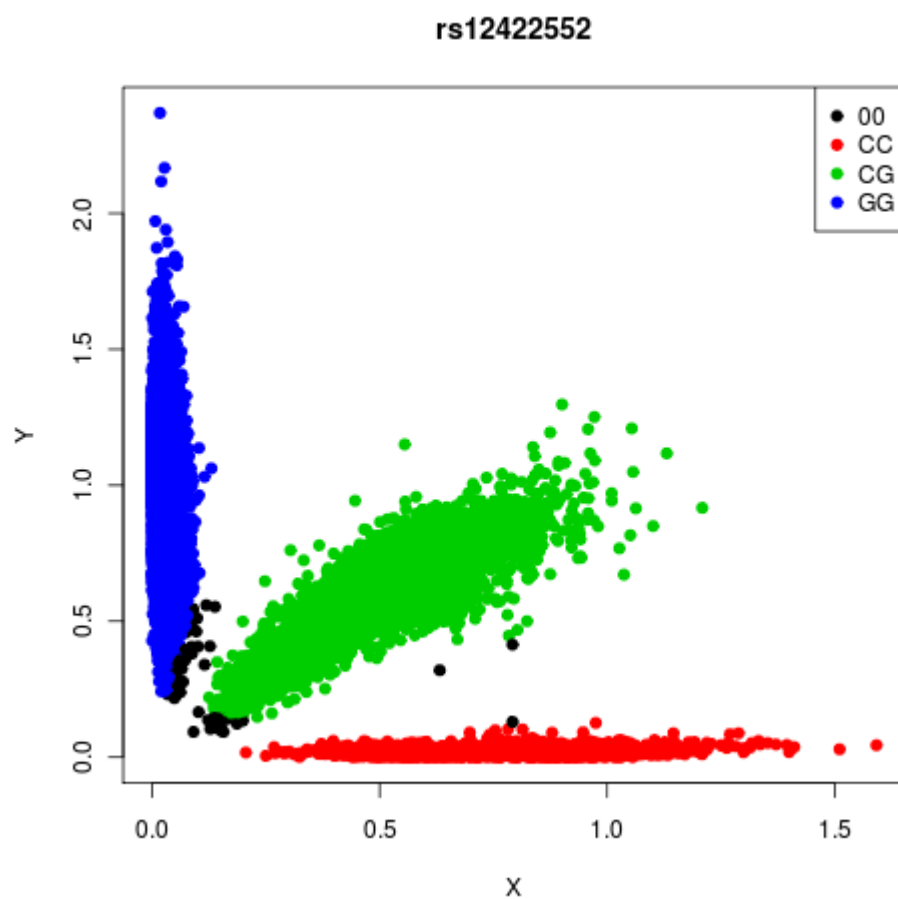
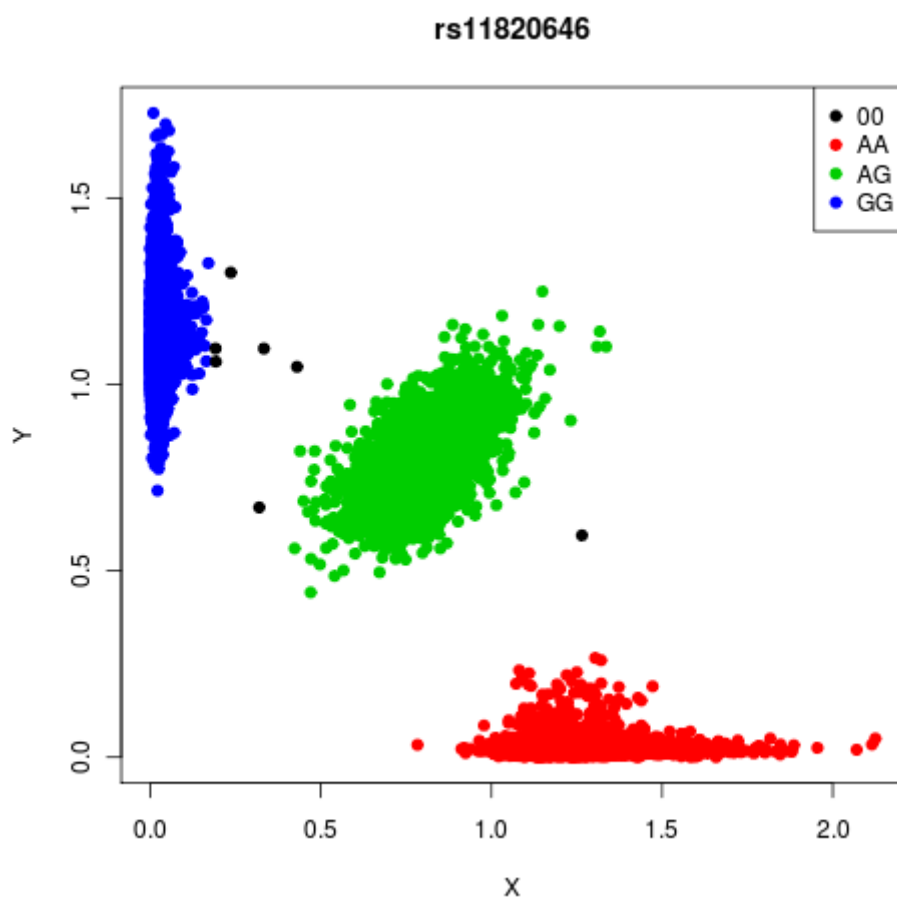


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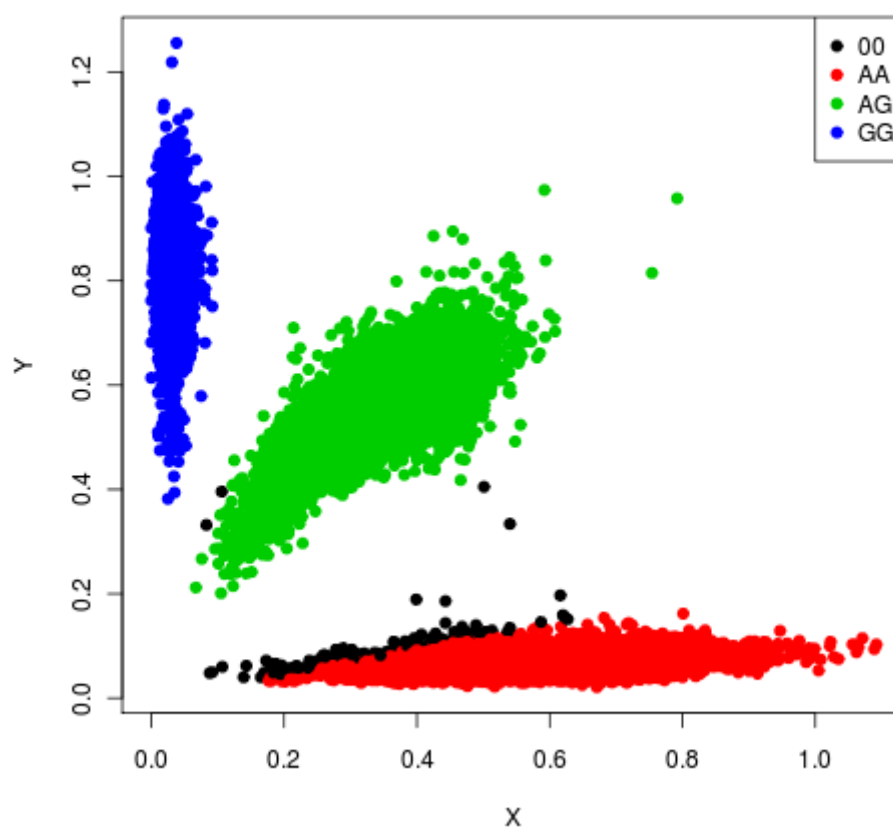


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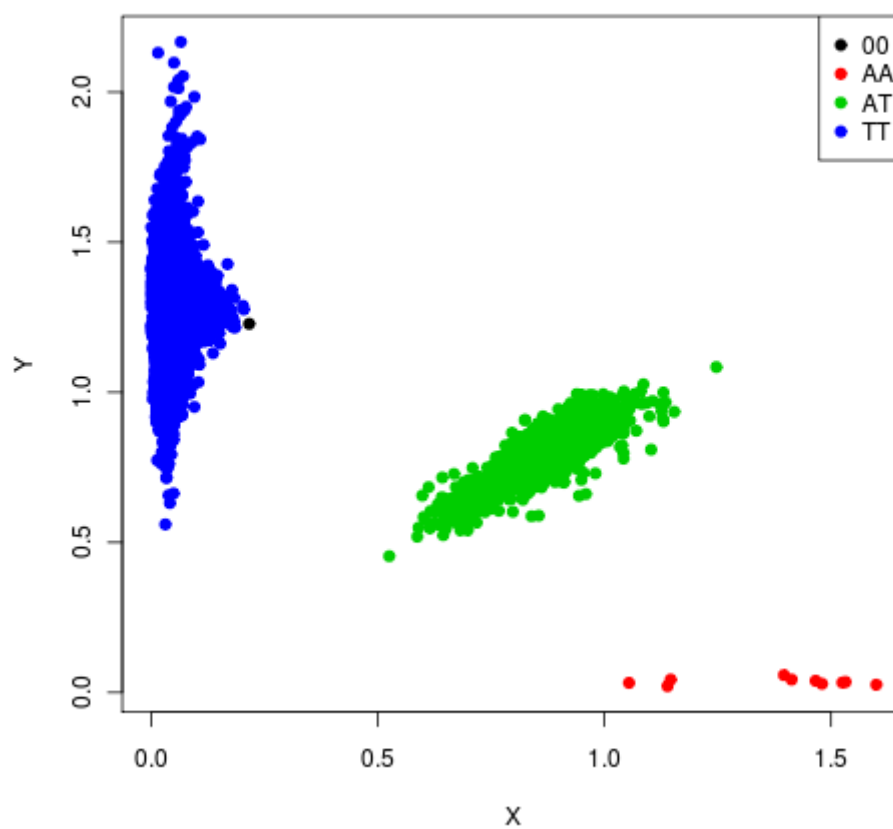


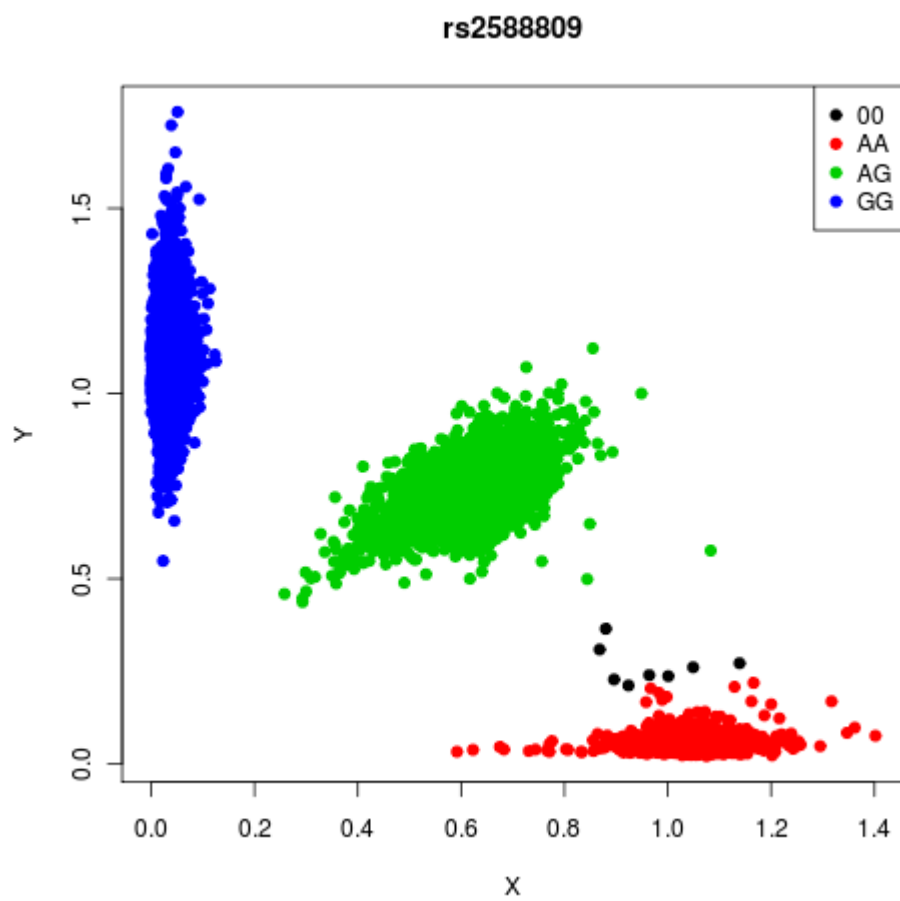
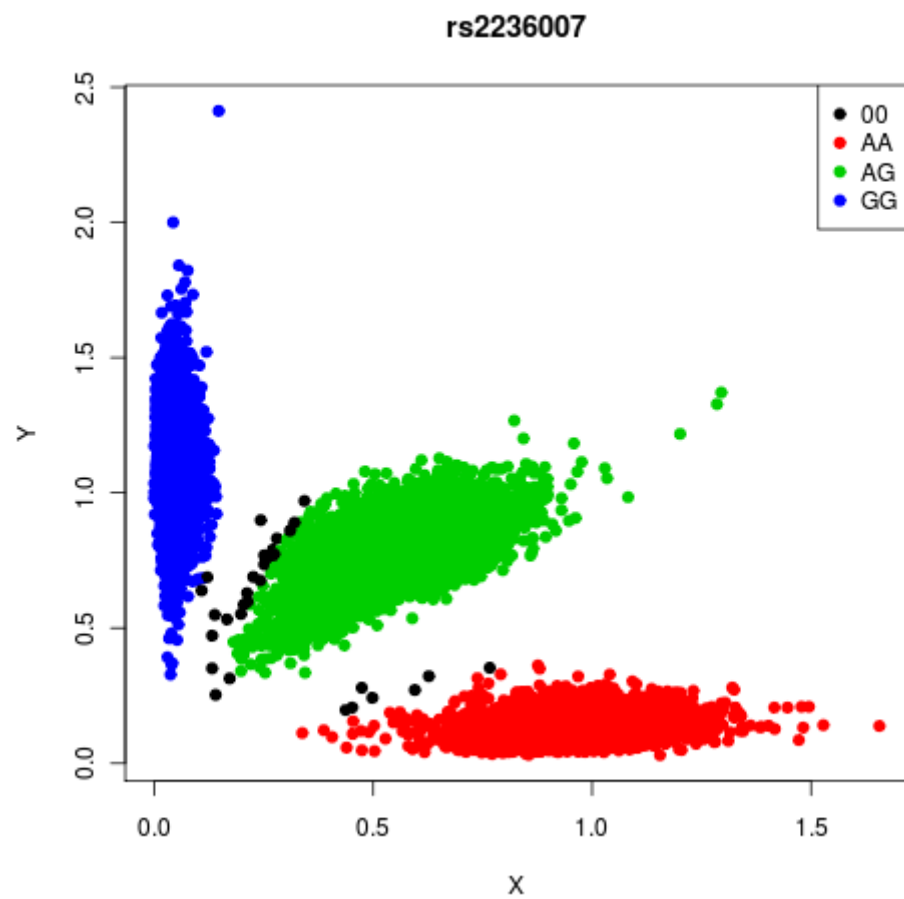


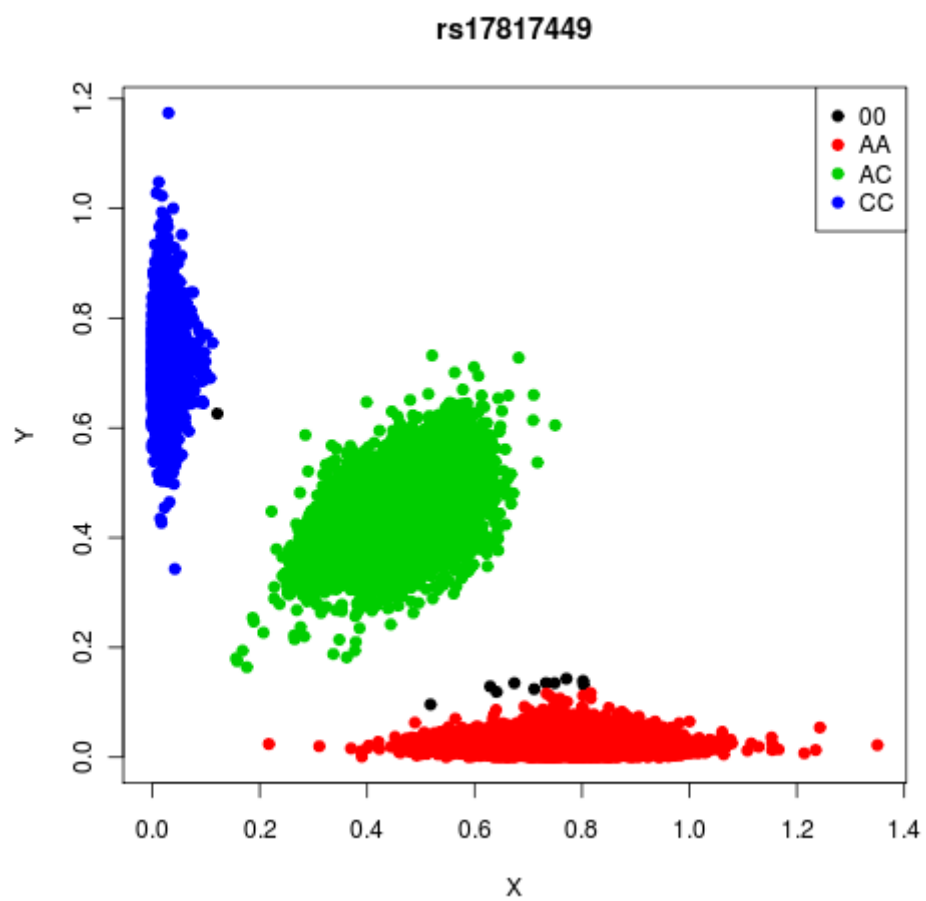
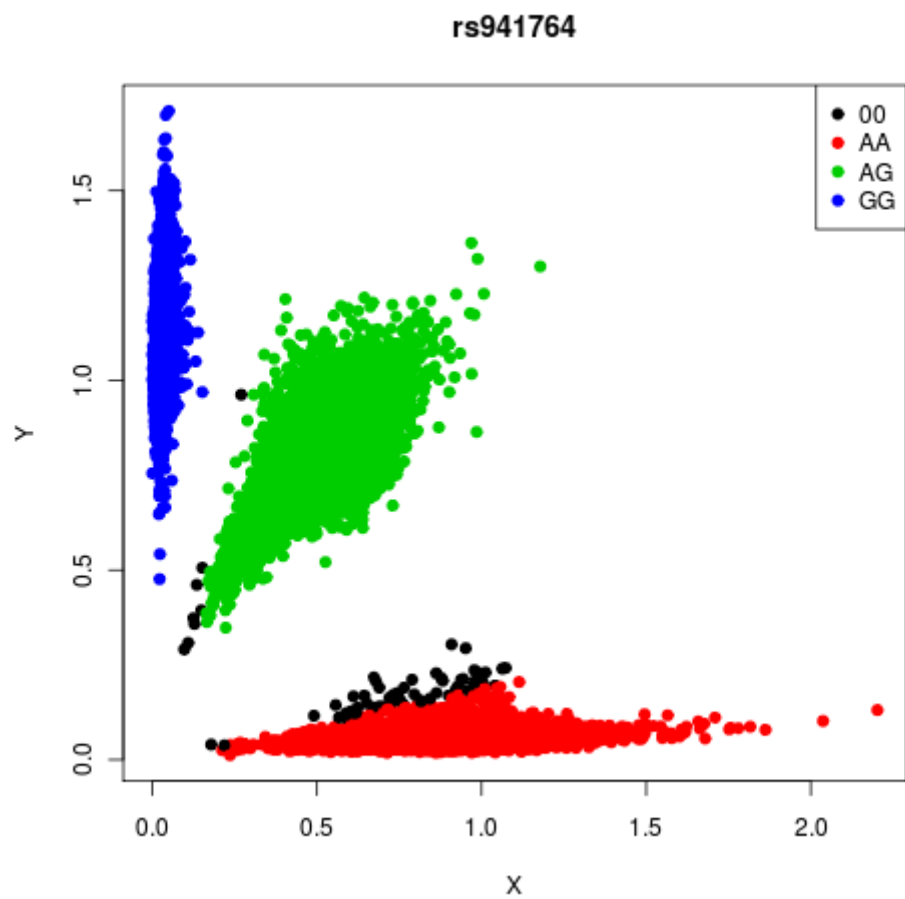
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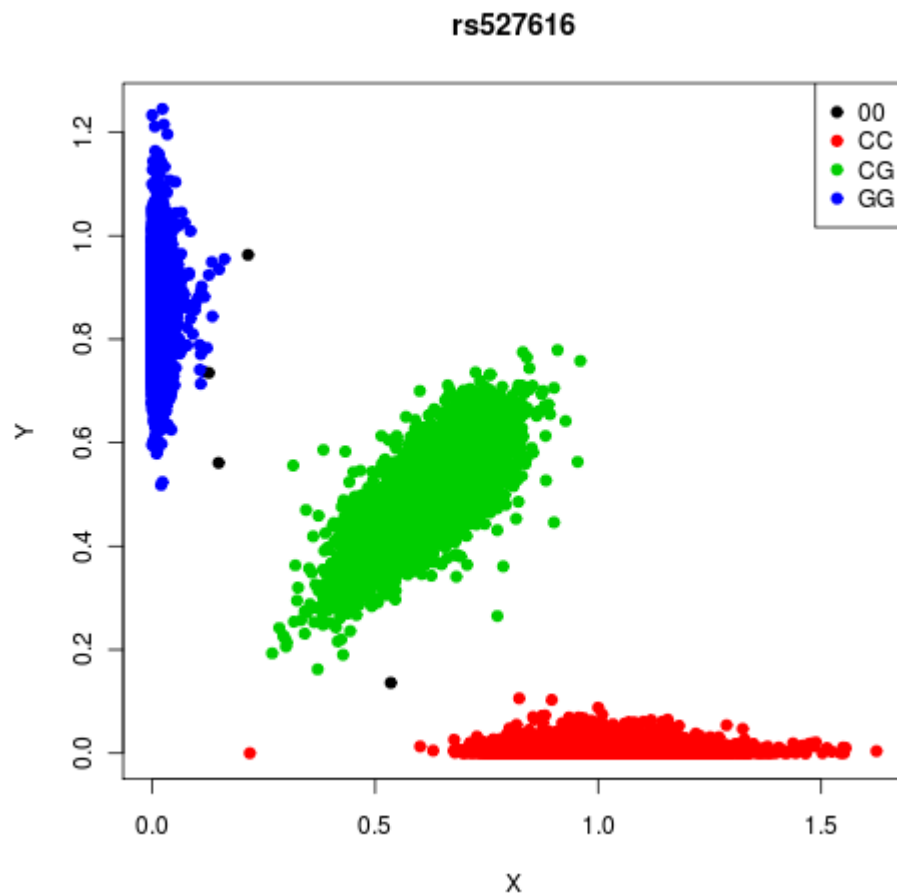
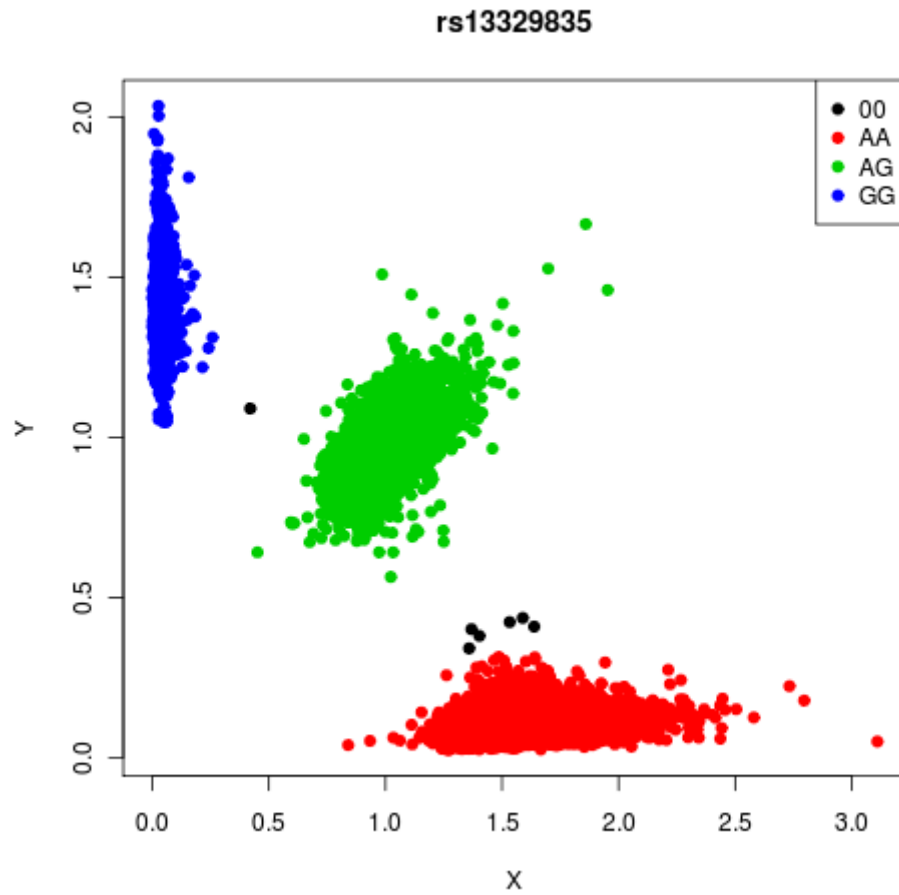


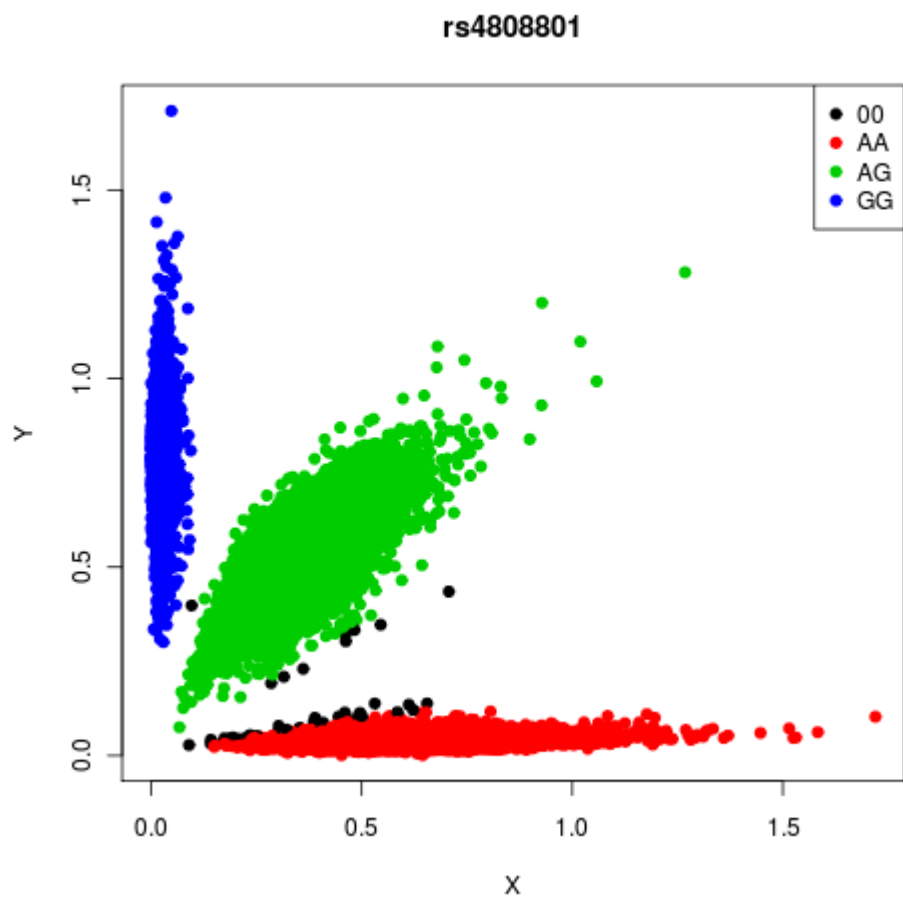
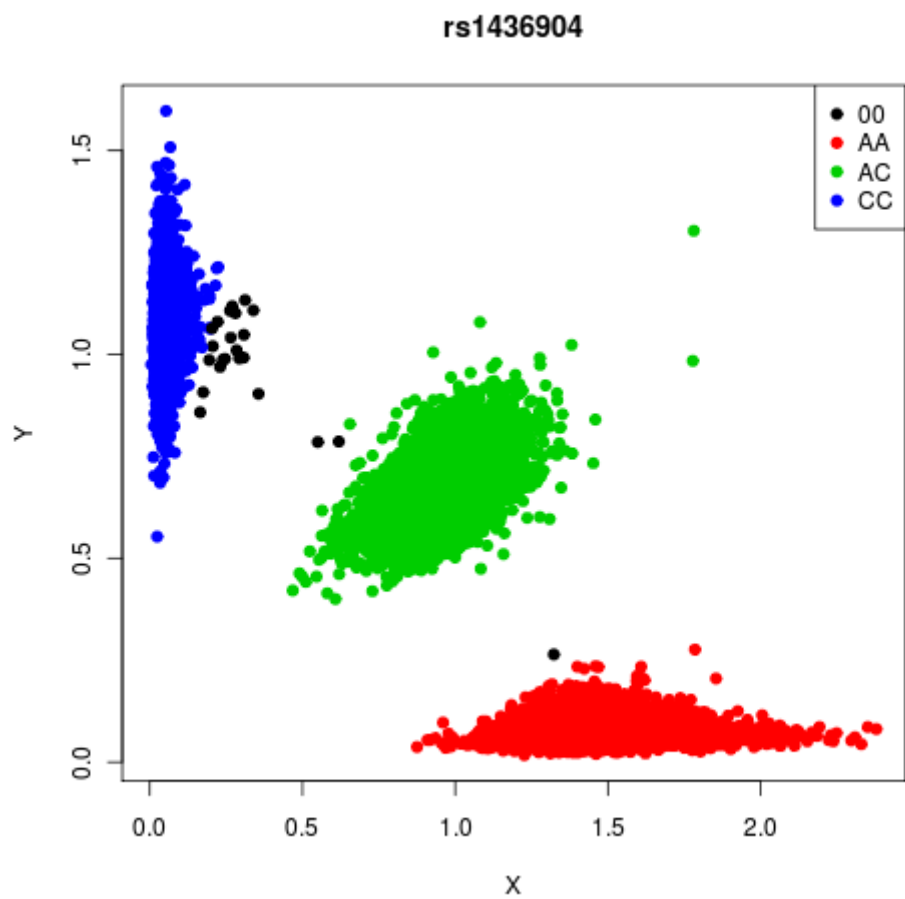
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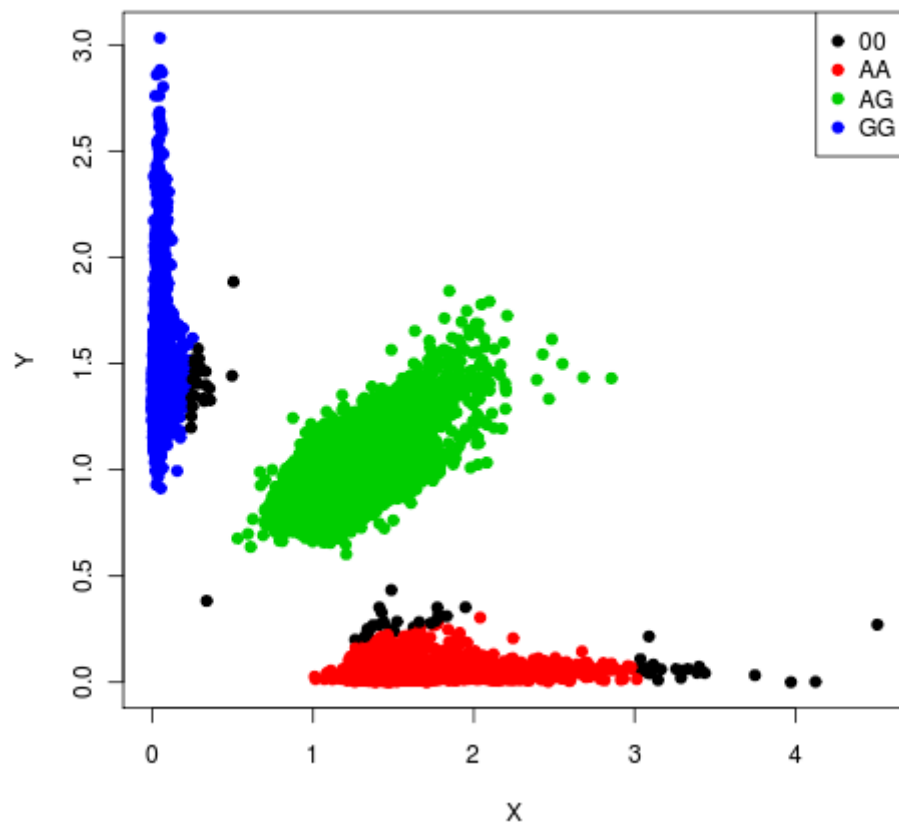




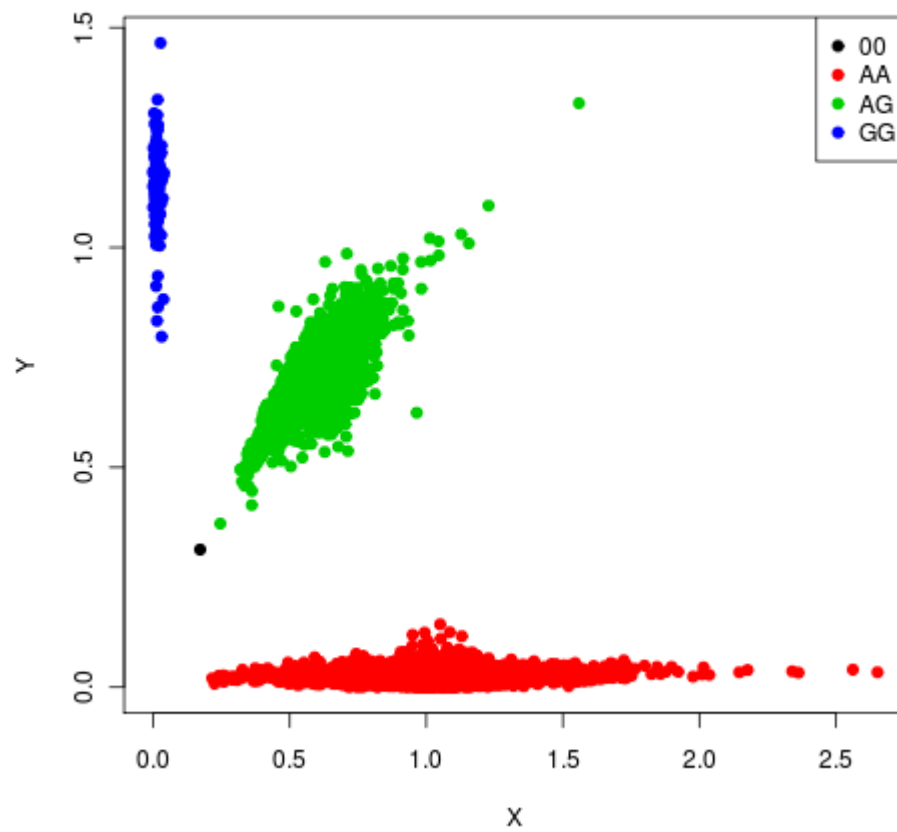




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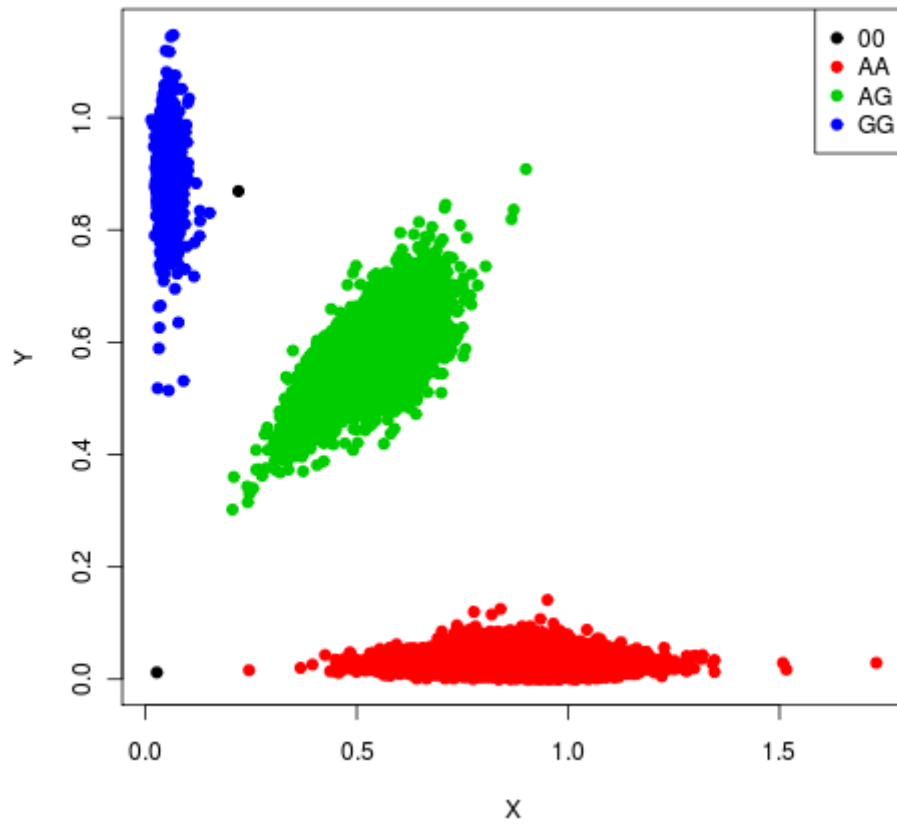


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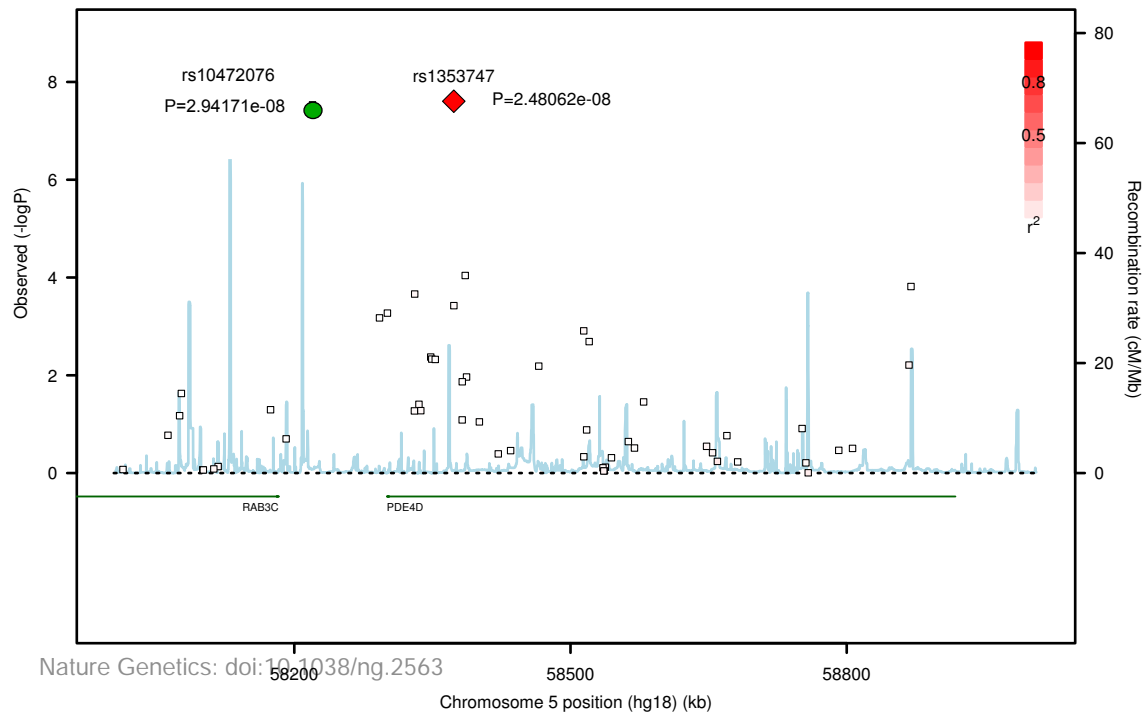
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**Supplementary Figure 4.** Regional association plots for 4 regions containing two independent SNPs each reaching  $P < 5 \times 10^{-8}$  in the combined GWAS+iCOGS analysis. Plots show the  $-\log_{10}$  association  $P$  values of SNPs, the build 36/hg18 coordinates in kilobases, recombination rates and genes in the region. The intensity of red shading indicates the strength of LD ( $r^2$ ) with the index SNP (shown as red diamond). The green circle denotes the second independent SNP. Plots drawn with a modified Rscript from <http://www.broadinstitute.org/mpg/snap/ldplot.php>. (a) 5q11.2 (b) 8q21.11 (c) *DNAJC1* (d) 18q11.2.

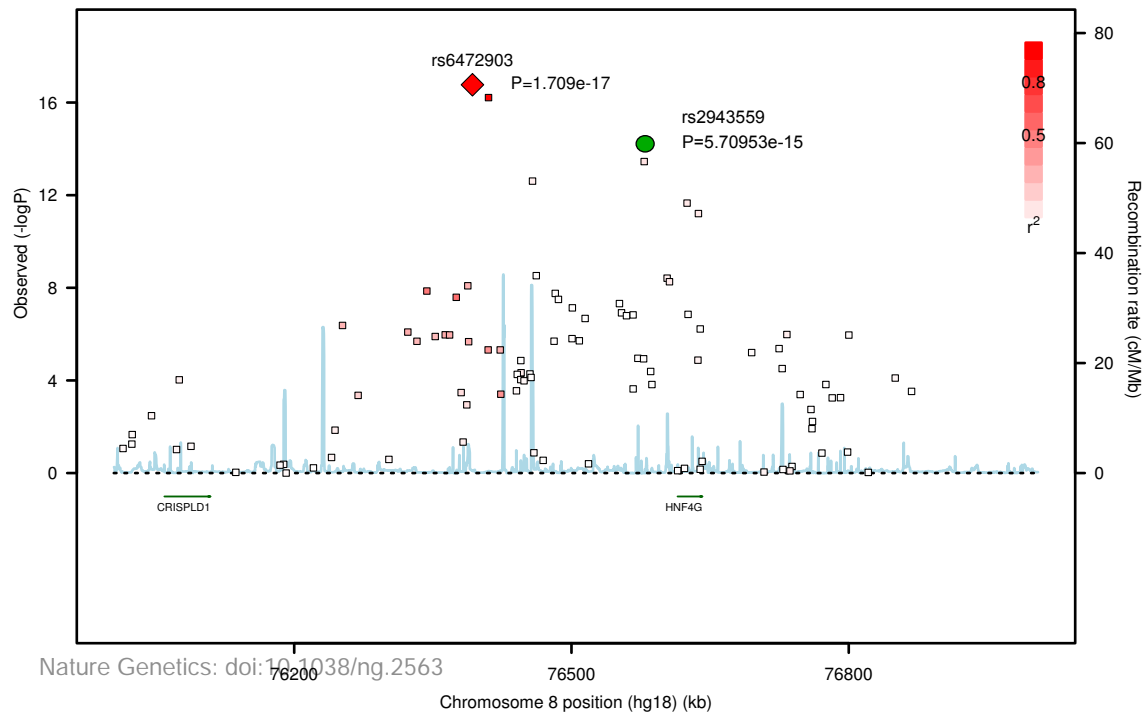
(a) 5q11.2

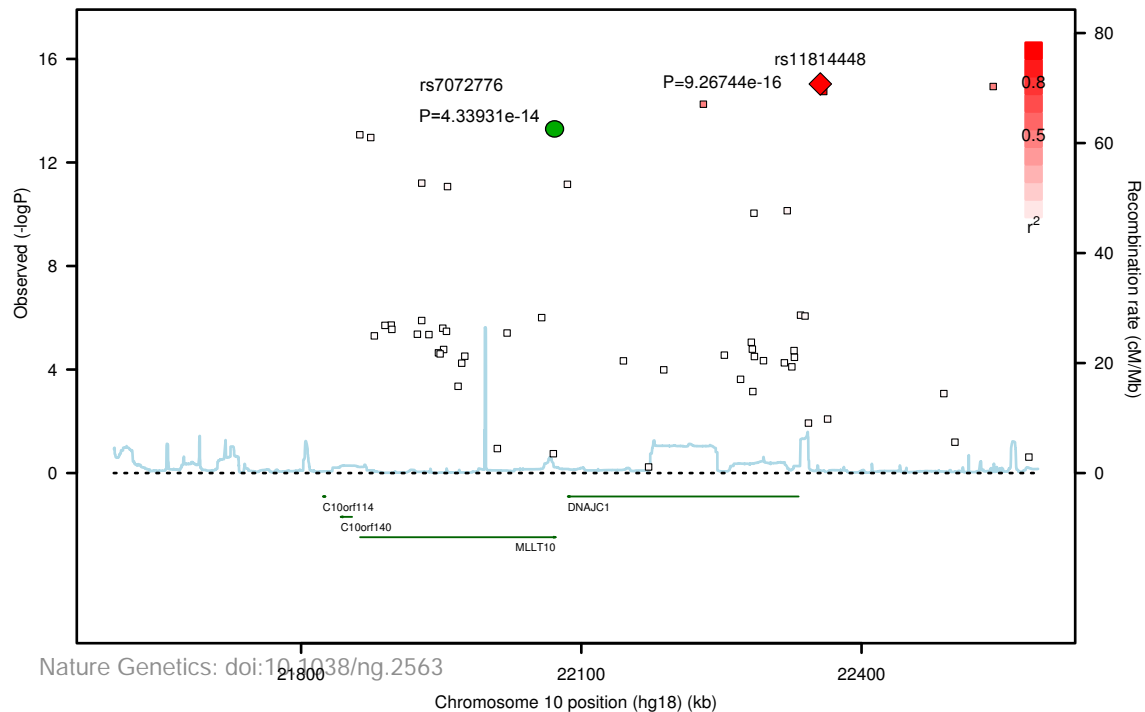
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(b) 8q21.11

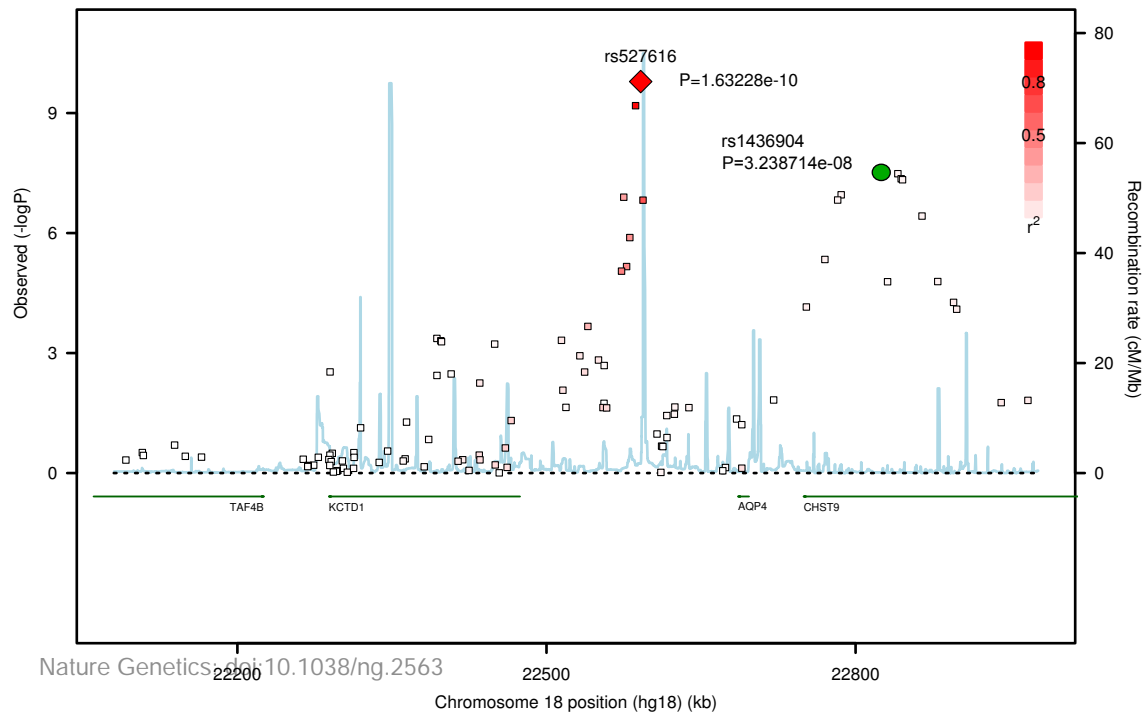
rs6472903 ( CEU )





(d) 18q11.2

rs527616 ( CEU )



## Supplementary Tables

**Supplementary Table 1.** Genome-wide association studies (GWAS) contributing to the current analysis.

Study	Country	Case ascertainment	Control ascertainment	Genotyping platform	Cases <sup>1</sup>	Controls <sup>1</sup>	Reference
ABCFS/kConFab	Australia	Recruitment through cancer registries in Victoria and New South Wales	Recruitment from the electoral rolls in Melbourne and Sydney matched to cases by age in-5 year categories	Illumina 610k	282	285	<sup>1</sup>
BBCS	UK	Recruitment through cancer registries and clinics in the UK, predominantly bilateral cases	WTCCC2: 1958 Birth Cohort + UK National Blood Service	Illumina 370k (cases) Illumina 1.2M (controls)	1609	5190	<sup>2</sup>
CGEMS	USA	Postmenopausal cases from Nurses Health Study	Individually matched controls from Nurses Health Study	Illumina 550k	1127	1130	<sup>3</sup>
GC-HBOC	Germany	BRCA1/2 mutation negative cases from University	KORA (Cooperative Health Research in	Affymetrix 5.0k (cases) Affymetrix 6.0k (controls)	634	477	<sup>4</sup>

Study	Country	Case ascertainment	Control ascertainment	Genotyping platform	Cases <sup>1</sup>	Controls <sup>1</sup>	Reference
		Clinics in Cologne and Munich	the Region Augsburg)				
MARIE	Germany	Random sample of cases from the MARIE study, but restricted to ductal and lobular carcinomas and oversampled for lobular (about 2:1)	KORA (Cooperative Health Research in the Region Augsburg)	Illumina 370k (cases) Illumina 550k (controls)	708	470	<sup>5</sup>
HEBCS	Finland	Unselected cases plus additional familial cases from Helsinki University Central Hospital	Population Controls from from the NordicDB, a Nordic pool and portal for genome-wide control data	Illumina 550k + 610k (cases) Illumina 370k (controls)	810	1012	<sup>6,7</sup>
SASBAC	Sweden	Population-based case control study of postmenopausal women	Population-based controls frequency matched by age to cases	Illumina 317k+240k (cases) Illumina 550k (controls)	790	756	<sup>6</sup>
UK2	UK	UK cancer genetics clinics + oncology clinics	WTCCC2: 1958 Birth Cohort + UK National Blood Service	Illumina 670k (cases) Illumina 1.2M (controls)	3628	5190	<sup>8</sup>



Study	Country	Case ascertainment	Control ascertainment	Genotyping platform	Cases <sup>1</sup>	Controls <sup>1</sup>	Reference
DFBBCS	Netherlands	BRCA1/2 mutation negative familial bilateral breast cancer patients selected from five clinical genetics centers; Erasmus University Medical Center/Daniel den Hoed, The Netherlands Cancer Institute, Leiden University Medical Center, University Medical Center Utrecht, and VU University Medical Center.	Controls were from the Rotterdam study, and are 55 years or older at the time of inclusion. For this study females were selected and breast cancer cases were excluded.	Illumina 610k (cases) Illumina 550k (controls)	464	3255	<sup>9</sup>

<sup>1</sup>Final numbers used in the analysis, after QC.

**Supplementary Table 2.** Participating studies in BCAC contributing to the COGS replication phase.

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
STUDIES OF WHITE EUROPEAN WOMEN						
ABCFR	Australian Breast Cancer Family Study <sup>1</sup>	Australia	Cancer registries in Victoria and New South Wales (1992-1999): all cases from Melbourne and Sydney diagnosed before age 40 plus a random sample of those diagnosed at ages 40-59.	Identified between 1992-1999 from the electoral rolls in Melbourne and Sydney (enrolling to vote is compulsory); frequency matched to cases by age in-5 year categories.	643	551
ABCS	Amsterdam Breast Cancer Study <sup>10</sup>	Netherlands	Breast cancer patients diagnosed before age 50 in 2003-2009 at the NKI-AVL; and (ABCS-F) All non-BRCA1/2 breast cancer cases from the family cancer clinic of the NKI-AVL tested in the period 1995-2009; all ages and diagnosed with breast cancer in 1965-2008.	Population-based cohort of women recruited through the Sanquin blood bank, all ages.	1264	1429
BBCC	Bavarian Breast Cancer Cases and Controls <sup>11</sup>	Germany	Consecutive, unselected cases with invasive breast cancer recruited at the University Breast Centre, Franconia in Northern Bavaria from 2002-2010.	Healthy women aged 55 or older with no diagnosis of cancer. Invited by a newspaper advertisement in Northern Bavaria between 2002-2010.	564	458
BBCS	British Breast Cancer Study <sup>2</sup>	U.K.	(i) English & Scottish Cancer Registries: all breast cancer cases who developed a first primary before age 66 in 1971 or later and who subsequently developed a second primary cancer. (ii) Breast Cancer Clinics: all breast cancer cases who developed a first primary before age 71 in 1967 or later and who either subsequently developed a second primary or had at least two affected female first-degree relatives. All recruited from 2001-2008.	A friend, sister-in-law, daughter-in-law or other non-blood relative of cases, recruited from 2001-2008.	1507	1397

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
BIGGS	Breast Cancer in Galway Genetic Study <sup>12</sup>	Ireland	Unselected cases recruited from University College Hospital Galway and surrounding hospitals in the West of Ireland since 2001	Women > 60 years with no personal history of any cancer and no family history of breast or ovarian cancer identified from retirement groups in the West of Ireland between 2001-2008.	836	719
BSUCH	Breast Cancer Study of the University Clinic Heidelberg <sup>13</sup>	Germany	All cases diagnosed with breast cancer in 2007-2009 at the University Women's Clinic Heidelberg.	Female blood donors recruited in 2007-2009 at the Institute of Transfusion Medicine & Immunology, Mannheim.	848	954
CECILE	CECILE Breast cancer study <sup>14</sup>	France	All cases diagnosed with breast cancer in 2005-2007 among women <75 years of age residing in the <i>départements</i> of Ille-et-Vilaine and Côte d'Or . Cases were recruited from the main cancer treatment center (Centre Eugène-Marquis in Rennes and Centre Georges-François-Leclerc in Dijon) and from other private or public hospitals in each area.	General population control women residing in the same areas as the cases (Ille-et-Vilaine and Côte d'Or). Controls were frequency-matched to the cases by 5-year age groups. They were recruited in 2005-2007 using a random digit dialing procedure and quotas by socioeconomic status to reflect the distribution by SES of the population in each area.	1019	999
CGPS	Copenhagen General Population Study <sup>15</sup>	Denmark	Consecutive, incident cases from one hospital with centralized care for a population of 400,000 women in Copenhagen (2001-present).	Women with no history of breast cancer residing in the same region as cases identified from the Copenhagen General Population Study (2003-2007).	2901	4086
CNIO-BCS	Spanish National Cancer Centre Breast Cancer Study <sup>16</sup>	Spain	(i) consecutive breast cancer patients from three public hospitals, two in Madrid and one in Oviedo; (ii) cases with at least one affected first degree relative recruited through the CNIO family cancer clinic in Madrid (2000-2005).	Women attending the Menopause Research Centre, Madrid and female members of the College of Lawyers attending a free, targeted medical check-up in Madrid, all free of breast cancer and all in Madrid between	902	876

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
				2000-2005.		
CTS*	California Teachers Study <sup>17</sup>	USA	Nested case-control study conducted within a cohort of California teachers (113,590) who were under age 80 years at baseline, had no prior history of invasive or <i>in situ</i> breast cancer. Cases are women newly diagnosed with a histologically confirmed invasive primary adenocarcinoma of the breast at age 80 years or younger from 1998 to 2008.	Controls are a probability sample of at-risk cohort members, frequency matched to cases on age at baseline (5-year age groups), self-reported race/ethnicity (white, African American, Latina, Asian, other), and broad geographic region within California. Controls were selected without replacement, using an assigned reference date.	69	70
DEMOKRITOS*	DEMOKRITOS	Greece	Triple negative breast cancer cases enrolled from 1997-2010 in hospitals serving geographical areas of Greece, including Athens metropolitan area, Thessaloniki, Ioannina, Patras, and Crete (Chania), in collaboration with the Hellenic Cooperative Oncology Group (HECOG).	Regional controls from Athens, Greece were population-based unaffected women of the same age range.	413	95
ESTHER	ESTHER Breast Cancer Study <sup>18</sup>	Germany	Breast cancer cases in all hospitals in the state of Saarland, from 2001-2003 (ESTHER) and 1996-1998 (VERDI).	Random sample of women a routine health check-up in Saarland, in 2000-2002; frequency matched to cases by age in 5-year categories.	478	502
GENICA	Gene Environment Interaction & Breast Cancer in Germany <sup>19, 20</sup>	Germany	Incident breast cancer cases enrolled at hospitals in the Greater Bonn area between 2000-2004.	Random address sample selected in 2001-2004 from 31 population registries in the greater Bonn area; frequency matched to cases on year of birth in 5-year categories.	464	427
HEBCS	Helsinki Breast Cancer Study	Finland	(1) Consecutive cases (883) from the Department of Oncology, Helsinki University Central Hospital	Healthy females from the same geographical region in Southern		

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
			1997-8 and 2000, (2) Consecutive cases (986) from the Department of Surgery, Helsinki University Central Hospital 2001 – 2004, (3) Familial breast cancer patients (536) from the Helsinki University Central Hospital, Departments of Oncology and Clinical Genetics (1995-).	Finland in 2003.	1658	1233
HMBCS	Hannover-Minsk Breast Cancer Study <sup>21</sup>	Belarus	Cases from the Byelorussian Institute for Oncology and Medical Radiology Aleksandrov N.N. in Minsk or at one of 5 regional oncology centers in Gomel, Mogilev, Grodno, Brest or Vitebsk (2002-2008).	Women attending general medical examination at gynecology clinics in Gomel, Mogilev, Grodno, Brest or Vitebsk; women attending the Institute for Inherited Diseases in Minsk; female blood donors in Minsk; healthy relatives of cases (2002-2008).	690	130
KARBAC	Karolinska Breast Cancer Study	Sweden	1. Familial cases from Department of Clinical Genetics, Karolinska University Hospital, Stockholm. 2. Consecutive cases from Department of Oncology, Huddinge & Söder Hospital, Stockholm 1998-2000.	Blood donors of mixed gender from same geographical region. Excess material was received from all blood donors over a 3 month period in 2004 (approximately 3000) and DNA was extracted from a random sample of 1500.	722	662
KBCP	Kuopio Breast Cancer Project <sup>22</sup>	Finland	Women seen at Kuopio University Hospital between 1990-1995 because of a breast lump, mammographic abnormality, or other breast symptom and who were found to have breast cancer.	Selected from the National Population Register between 1990-1995; age and long-term area-of-residence matched to cases.	445	251
kConFab/AOCS	Kathleen Cuninghame Foundation Consortium for Research into Familial Breast Cancer / Australian Ovarian	Australia	Index (youngest affected) cases from <i>BRCA1</i> - and <i>BRCA2</i> -mutation-negative multiple-case breast and breast-ovarian families recruited through family cancer clinics from across Australia and New Zealand from 1998-present.	Identified from the electoral rolls from across Australia as part of the Australian Ovarian Cancer Study in 2002-2006.	575	897

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
	Cancer Study <sup>23</sup>					
LMBC	Leuven Multidisciplinary Breast Centre <sup>24</sup>	Belgium	All patients diagnosed with breast cancer and seen in the Multidisciplinary Breast Center in Leuven (Gashuisberg) since June 2007 plus retrospective collection of cases diagnosed since 2000.	Blood donors at Gasthuisberg Hospital (200-2008).	2671	1388
MARIE	Mammary Carcinoma Risk Factor Investigation <sup>5</sup>	Germany	Incident cases diagnosed from 2001-2005 in the study region Hamburg in Northern Germany, and from 2002-2005 in the study region Rhein-Neckar-Karlsruhe in Southern Germany.	2 controls per case were randomly drawn from population registries and frequency matched by birth year and study region to the case. Controls were recruited from 2002 to 2006.	1796	1778
MBCSG	Milan Breast Cancer Study Group <sup>25</sup>	Italy	Familial and/or early onset breast cancer patients (aged 22-87) negative for mutations in <i>BRCA1</i> and <i>BRCA2</i> , ascertained at two large cancer centers in Milan from 2000-present.	Female blood donors recruited at two centres in Milan from 2004-present and 2007-present.	488	400
MCBCS	Mayo Clinic Breast Cancer Study <sup>26</sup>	U.S.A.	Incident cases residing in 6 states (MN, WI, IA, IL, ND, SD) seen at the Mayo Clinic in Rochester, MN from 2002-2010.	Women presenting for general medical examination at the Mayo Clinic from 2002-2010; frequency matched to cases on age, ethnicity and county/state.	1862	1931
MCCS	Melbourne Collaborative Cohort Study <sup>27</sup>	Australia	Incident cases from the cohort of 24,469 women, diagnosed during the follow-up from baseline (1990-1994) to 2008.	Random sample of the initial cohort.	614	511
MEC	Multiethnic Cohort	USA	Incident cases identified from SEER cancer registries in Los Angeles County & State registries in California & Hawaii, USA from 1993-2002. Grouped by self-reported ethnicity.	Women without cancer from the same States, recruited concurrently with cases & frequency matched to cases by age at blood-draw & self-reported ethnicity.	731	741
MTLGBCS	Montreal Gene-Environment Breast	Canada	All cases are postmenopausal women (47-75 years) living in Montreal with a primary invasive	Random sample from the universal Provincial Voter Registration List,	489	436

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
	Cancer Study		breast cancer and with no previous occurrence of any type of cancer. All cases were identified from 2007 to 2010 in 15 of 16 Montreal hospitals that treat breast cancer.	approximately frequency-matched to cases on age (5-year bins) and living in Montreal.		
NBCS*	Norwegian Breast Cancer Study <sup>28</sup>	Norway	Incidence cases from three different hospitals: Ullevål Univ. Hospital 1990-94, Norwegian Radium Hospital 1975-1986 and 1995-1998, Haukeland Univ. Hospital 1992-2001.	Women residing in Tromsø and Bergen who attended the Norwegian Breast Cancer Screening Program.	22	70
NBHS_TN*	Nashville Breast Health Study (Triple Negative)	U.S.A.	Triple negative invasive breast cancer cases from a collection of Invasive breast cancer or ductal carcinoma in situ cases between the ages of 25 and 75 years (2001-2010). Cases were identified from participating hospitals in the Nashville Metropolitan area and the Tennessee Cancer Registry (TCR).	Controls were recruited through random digit dialing.	125	118
OBCS	Oulu Breast Cancer Study <sup>29</sup>	Finland	Consecutive incident cases diagnosed at the Oulu University Hospital between 2000-2004.	Female blood donors recruited in 2002 from the same geographical region in Northern Finland.	507	414
OFBCR	Ontario Familial Breast Cancer Registry <sup>30</sup>	Canada	Invasive cases aged 20-54 years identified from the Ontario Cancer Registry from 1996-1998. All those at high genetic risk were eligible; random samples of women not meeting these criteria were also asked to participate.	Identified by calling randomly selected residential telephone numbers in the same geographical region from 1998-2001; frequency matched to cases by age in 5 year categories.	1175	511
ORIGO	Leiden University Medical Centre Breast Cancer Study <sup>31, 32</sup>	Netherlands	Consecutive case patients diagnosed 1996–2006 in 2 hospitals in South–West Netherlands (Leiden & Rotterdam). No selection for family history; Rotterdam case patients selected for diagnosis aged <70. Case patients with in situ carcinomas	(1) Blood bank healthy donors from Southwest Netherlands recruited in 1996, 2000 or 2007; (2) People who married a person who was part of a family with high breast cancer risk		

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
			eligible.	(BRCA1/2/x). From the Southwest of the Netherlands, recruited 1990–1996; (3) Females tested at the local clinical genetics department for familial diseases, excluding familial cancer syndromes (no mutation found in gene(s) related to the disease being tested), recruited 1995–2007.	357	327
OSU*	The Stefanie Spielman Breast Bank and the Columbus Area Control Sample Bank	U.S.A.	Incident triple negative breast cancer cases enrolled at The Ohio State University James Comprehensive Cancer Center between 2003 and 2011.	Controls were chosen from an existing bank of individuals seen for routine health issues at primary care and internal medicine clinics, recruited 2007-2011. They were age and ethnicity frequency matched to cases.	207	203
PBCS	NCI Polish Breast Cancer Study <sup>33</sup>	Poland	Incident cases identified through a rapid identification system in participating hospitals covering ~ 90% of all eligible cases, and cancer registries in Warsaw and Łódź covering 100% of all eligible cases (2000-2003).	Randomly selected from population lists of all residents of Poland from 2000-2003, stratified and frequency matched to cases on city and age in 5-year categories.	519	424
pKARMA	Karolinska Mammography Project for Risk Prediction of Breast Cancer - prevalent cases	Sweden	Incident cases from Jan 2001 – Dec 2008 from the Stockholm/Gotland area. Identified through the Stockholm breast cancer registry.	Unmatched participants of the KARMA mammography screening study recruited between 2010 and 2011 from Helsingborg and Stockholm.	5428	5537
RBCS	Rotterdam Breast Cancer Study <sup>34</sup>	Netherlands	Familial breast cancer patients selected from the clinical genetics center at Erasmus Medical Center between 1994-2005.	Spouses or mutation-negative siblings of heterozygous Cystic Fibrosis mutation carriers selected from the clinical genetics centre at	664	699



Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
				Erasmus Medical Center between 1996-2006.		
RPCI*	Roswell Park Cancer Institute	U.S.A	Triple negative invasive breast cancer cases from incident cases recruited to the RPCI Data Bank and Biorepository.	Healthy controls identified from employee volunteers, and women recruited from community events.	136	126
SASBAC	Singapore and Sweden Breast Cancer Study <sup>35</sup>	Sweden	Women diagnosed in Sweden aged 50-74 in 1993-1995.	Population-based controls frequency matched by age to the cases.	397	661
SBCS	Sheffield Breast Cancer Study <sup>36</sup>	U.K.	Women with breast cancer recruited in 1998-2005 at surgical outpatient clinics at the Royal Hallamshire Hospital, Sheffield.	Unselected women attending the Sheffield Mammography Screening Service in 2000-2004 with no evidence of a breast lesion.	839	848
SEARCH	Study of Epidemiology & Risk Factors in Cancer Heredity <sup>37</sup>	U.K.	Identified through the Eastern Cancer Registration and Information Centre: (i) prevalent cases; diagnosed 1991-1996; under 55 years of age at diagnosis; recruited 1996-2002 (ii) incidence cases; diagnosed since 1996; under 70 years of age at diagnosis; recruited 1996-present.	(a) Women from the same geographic region selected from the EPIC-Norfolk cohort study, 1992-1994 (b) women attending GP practices, frequency matched to cases by age and geographic region (2003-present) (c) women attending for breast screening as part of the NHSBSP participating in the Sisters in Breast Screening (SIBS) study	9294	8068
SKKDKFZ*	Städtisches Klinikum Karlsruhe Deutsches Krebsforschungszentrum Study <sup>38</sup>	Germany	Women diagnosed with primary <i>in situ</i> or invasive breast cancer at the Städtisches Klinikum Karlsruhe from March 1993 to July 2005. Cases were 21-93 years of age.	<i>Controls selected from GC-HBOC</i>	136	168
SZBCS	IHCC-Szczecin Breast Cancer Study <sup>39</sup>	Poland	Prospectively ascertained cases of invasive breast cancer patients diagnosed at the Regional Oncology Hospital (2002-2003 and 2006-2007) or the University Hospital (2002-2007), both in Szczecin, West Pomerania, Poland.	Selected from a population-based study of the 1.3 million inhabitants of West Pomerania (2003-2004); matched to cases for year of birth, sex and region.	365	315

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
UKBGS	Breakthrough Generations Study <sup>40</sup>	UK	Cohort members who had had breast cancer or in situ breast cancer before entry into the Breakthrough Generations Study (cohort of >100,000 women followed up for breast cancer, recruited from the UK during 2003-2011).	Women who had not had breast cancer or in situ breast cancer before entry into the cohort study selected by 1:1 matching to cases on date of birth, year of entry in to the study (2003-2009), source of recruitment, availability of blood sample and ethnicity.	470	470
<b>STUDIES OF ASIAN WOMEN</b>						
ACP	Asian Cancer Project	Thailand	Cases from oncology centres in Thailand that underwent biopsy and had been pathologically diagnosed as having breast cancer.	Hospital based controls are women who were admitted to the same hospital as the cases with diseases not related to cancer or metabolic syndromes such as diabetes, heart diseases or conditions related to gynaecology.	423	636
HERPACC	Hospital-based Epidemiologic Research Program at Aichi Cancer Center <sup>41</sup>	Japan	Incident breast cancer cases who first visited Aichi Cancer Center between 2001 and 2005 and were diagnosed within 1 year from the first visit. No previous history of any type of cancer.	Controls were selected from pool of non-cancer patients who firstly visited Aichi Cancer Center between 2001-2005. Non-cancer status is defined as "having no positive finding on any of clinical/laboratory/graphical examination within 1 year from their first visit. No previous history of cancer is allowed.	694	1376
LAABC	Los Angeles County Asian-American Breast Cancer Case-Control	USA	Incident cases recruited from 1995-2007 and identified from SEER cancer registries in Los Angeles County. Grouped by self-reported	Controls were recruited during 1995-2009 and selected from the same neighbourhood as where cancer	812	990

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
	Study <sup>42</sup>		ethnicity.	cases resided at the time of diagnosis. Controls were frequency-matched to the cases on specific Asian ethnicities and 5-year age groups		
MYBRCA	Malaysian Breast Cancer Genetic Study <sup>43</sup>	Malaysia	Breast cancer cases identified at the Breast Cancer Clinic in University Malaya Medical Centre Jan 2001-July 2010; cases are a mixture of prevalent and incident cases	Controls are cancer-free individuals (21-70 years) with no breast or ovarian cancer in first degree relatives, randomly selected from women attending same hospital.	770	610
SBCGS	Shanghai Breast Cancer Genetic Study <sup>44</sup>	China	Newly-diagnosed breast cancer cases recruited from 1996 -2009. Cases were identified mostly from the Shanghai Cancer Registry. Some cases were identified from the Shanghai Women's Health Study.	Community controls randomly selected from the general population using the resident registry or from cancer-free cohort members in the Shanghai Women's Health Study. The controls were recruited from the same geographical region as cases during 1996-2009.	848	892
SEBCS	Seoul Breast Cancer Study <sup>45</sup>	South Korea	Consecutive, incident, cases from 2 hospitals in Seoul recruited between 2001-2005.	Women from same catchment area and participating in annual health check-up (2001-2005).	1162	1129
SGBCC	Singapore Breast Cancer Cohort	Singapore	Living breast cancer patients diagnosed with primary in-situ or invasive breast cancer at National University Hospital. Cases are a mixture of prevalent and incident cases.	All community-dwelling individuals who are Singaporeans or Singaporean Permanent Residents, 21 years and older. Exclusion criteria were a medical history of cancer, acute myocardial infarction or stroke, or major psychiatric morbidity including schizophrenia,	533	502

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
				psychotic depression, and advanced Alzheimer's Disease.		
TBCS	IARC-Thai Breast Cancer <sup>46</sup>	Thailand	Incident cases diagnosed at the National Cancer Institute (NCI) in Bangkok and Khon Kaen Hospital during 2002-2004.	Randomly selected women visiting hospital patients with diseases other than breast or ovarian cancer at NCI Bangkok and Khon Kaen Hospital during 2002- 2004).	138	253
TWBCS	Taiwanese Breast Cancer Study <sup>47</sup>	Taiwan	Incident cases diagnosed & treated at 2 major teaching hospitals in Taiwan between 2002-2005.	Randomly selected women attending a health examination at same hospitals between 2002-2005.	889	236
<b>STUDIES OF AFRICAN-AMERICAN WOMEN</b>						
SCCS	Southern Community Cohort Study <sup>48</sup>	USA	Incident cases (N=222) from 2002-2009 identified from 12 state cancer registries in southeastern US. Prevalent cases (N=493) identified by self-reported history of breast cancer reported on cohort enrollment survey.	Controls for the incident cases were individually matched on age (+/- 2 years), self-reported race, menopausal status, enrollment site, and date of sample collection (+/- 6 months). Controls for the prevalent cases were frequency matched on age (+/- 1 year) and enrollment site.	679	680
NBHS	Nashville Breast Health Study <sup>44</sup>	USA	Through a rapid case-ascertainment system, we identified newly-diagnosed breast cancer cases through the Tennessee State Cancer Registry and five major hospitals in the city that provide medical care for breast cancer patients. Eligible cases were women diagnosed with invasive breast cancer or ductal carcinoma in situ, who were between the ages of 25 and 75, had no prior history of cancer other than non-melanoma skin cancer, had a resident telephone, spoke English,	Controls were identified via random digit dialing (RDD) of households in the same geographic area as cases during 2001-2011. Eligibility criteria for controls were the same as cases with the exception that controls did not have a prior cancer diagnosis other than simple skin cancer. Controls were frequency matched to cases on 5-year age group, race, and	437	252

Study Acronym	Study Name [Reference]	Country	Recruitment base		Sample size Post quality control	
			Cases	Controls	Cases	Controls
			and who were able to provide consent to the study. Recruitment period was from 2001 to 2011. The recruitment for European Americans ended in 2008.	county of residence.		

\* CTS, NBCS and SKKDKFZ are studies in BCAC but genotyped as part of the triple negative consortium (TNBCC). Part of GENICA was also genotyped as part of TNBCC. DEMOKRITOS, NBHS\_TN, OSU and RPCI were additional non-BCAC studies included as part of the TNBCC.

**Supplementary Table 3.** Quality Control Exclusions.

SNPs	Number	Samples	Number
<b>Called</b>	<b>211,155</b>	<b>Initial</b>	<b>114,225</b>
Call rate <95%	5,402	Cryptic duplicate	210
Hardy-Weinberg $P < 10^{-7}$	3,522	Discordant duplicate	42
Concordance in duplicate samples <98%	10	Discordant with previous genotyping	702
Monomorphic	2,261	Concordant replicate	2629
		Relative Pair	1981
		Cross-study duplicate	130
		Substudy duplicate	145
		Male	298
		Excess heterozygosity ( $P < 10^{-6}$ )	670
		Ethnic outlier	1244
		Call rate <95%	1656
		Phenotypic exclusion	527
		<b>Samples post QC</b>	<b>103,991</b>
		Overlap with GWAS	1,880
<b>SNPs post QC</b>	<b>199961</b>	<b>Samples post QC (no GWAS overlap)</b>	<b>102,111</b>

**Supplementary Table 4.** Associations between previously reported breast cancer associated SNPs and breast cancer risk in the combined GWAS and iCOGS replication.

Locus	Original SNP <sup>1</sup>	Chr. <sup>2</sup>	Position <sup>3</sup>	Allele <sup>4</sup>	MAF <sup>5</sup>	Combined GWAS		iCOGS		Combined <i>P</i>
						Per allele OR <sup>6</sup> (95%CI)	Ptrend	Per allele OR <sup>6</sup> (95%CI)	Ptrend	
1p11.2	rs11249433	1	120982136	A/G	0.40	1.14 (1.10-1.19)	1.5x10 <sup>-10</sup>	1.09 (1.07-1.11)	3.0x10 <sup>-18</sup>	2.0x10 <sup>-26</sup>
2q35	rs13387042	2	217614077	A/G	0.49	0.83 (0.80-0.86)	3.2x10 <sup>-21</sup>	0.88 (0.86-0.90)	2.3x10 <sup>-39</sup>	2.2x10 <sup>-57</sup>
<i>CASP8</i>	rs1045485	2	201857834	G/C	0.13	0.90 (0.85-0.96)	.00077	0.97 (0.94-1.00)	0.054	.0013
<i>SLC4A7</i>	rs4973768	3	27391017	C/T	0.47	1.14 (1.09-1.18)	8.7x10 <sup>-11</sup>	1.10 (1.08-1.12)	1.2x10 <sup>-21</sup>	2.3x10 <sup>-30</sup>
<i>TERT</i>	rs10069690	5	1332790	C/T	0.26	1.04 (0.98-1.11)	0.15	1.06 (1.04-1.09)	1.7x10 <sup>-8</sup>	7.2x10 <sup>-9</sup>
5p12	rs10941679	5	44742255	A/G	0.25	1.17 (1.12-1.23)	5.1x10 <sup>-12</sup>	1.13 (1.10-1.15)	1.5x10 <sup>-27</sup>	1.7x10 <sup>-37</sup>
<i>MAP3K1</i>	rs889312	5	56067641	A/C	0.28	1.16 (1.11-1.21)	7.7x10 <sup>-12</sup>	1.12 (1.10-1.15)	1.8x10 <sup>-26</sup>	2.7x10 <sup>-36</sup>
6q14.1	rs17530068	6	82249828	A/G	0.22	1.09 (1.04-1.14)	.0003	1.05 (1.03-1.08)	3.6x10 <sup>-6</sup>	8.2x10 <sup>-9</sup>
<i>ESR1</i>	rs3757318	6	151955806	G/A	0.07	1.21 (1.13-1.31)	2.7x10 <sup>-7</sup>	1.16 (1.12-1.21)	8.2x10 <sup>-16</sup>	2.2x10 <sup>-21</sup>
<i>ESR1</i>	rs2046210	6	151990059	G/A	0.34	1.11 (1.07-1.16)	3.7x10 <sup>-7</sup>	1.08 (1.06-1.10)	4.8x10 <sup>-14</sup>	2.0x10 <sup>-19</sup>

Locus	Original SNP <sup>1</sup>	Chr. <sup>2</sup>	Position <sup>3</sup>	Allele <sup>4</sup>	MAF <sup>5</sup>	Combined GWAS		iCOGS		Combined <i>P</i>
						Per allele OR <sup>6</sup> (95%CI)	Ptrend	Per allele OR <sup>6</sup> (95%CI)	Ptrend	
8q24	rs13281615	8	128424800	A/G	0.41	1.10 (1.14-1.19)	6.1x10 <sup>-11</sup>	1.09 (1.07-1.12)	4.3x10 <sup>-19</sup>	9.6x10 <sup>-28</sup>
<i>CDKN2A/B</i>	rs1011970	9	22052134	G/T	0.17	1.10 (1.05-1.16)	0.00026	1.06 (1.03-1.08)	2.2x10 <sup>-5</sup>	5.5x10 <sup>-8</sup>
9q31	rs865686	9	109928299	T/G	0.38	0.89 (0.86-0.93)	1.9x10 <sup>-8</sup>	0.89 (0.88-0.91)	7.8x10 <sup>-28</sup>	9.5x10 <sup>-35</sup>
<i>ANKRD16</i>	rs2380205	10	5926740	C/T	0.44	0.94 (0.90-0.97)	0.00080	0.98 (0.96-1.00)	0.075	0.0021
<i>ZNF365</i>	rs10995190	10	63948688	G/A	0.16	0.84 (0.80-0.89)	9.8x10 <sup>-10</sup>	0.86 (0.84-0.88)	1.6x10 <sup>-28</sup>	1.3x10 <sup>-36</sup>
<i>ZMIZ1</i>	rs704010	10	80511154	C/T	0.38	1.12 (1.08-1.17)	5.7x10 <sup>-9</sup>	1.08 (1.06-1.10)	5.1x10 <sup>-15</sup>	7.4x10 <sup>-22</sup>
<i>FGFR2</i>	rs2981579	10	123327325	G/A	0.40	1.35 (1.29-1.40)	5.2x10 <sup>-49</sup>	1.27 (1.24-1.29)	5.9x10 <sup>-125</sup>	1.9x10 <sup>-170</sup>
<i>LSP1</i>	rs3817198	11	1865582	T/C	0.31	1.06 (1.01-1.10)	0.011	1.07 (1.05-1.09)	3.5x10 <sup>-10</sup>	1.5x10 <sup>-11</sup>
11q13	rs614367	11	69037945	C/T	0.15	1.31 (1.23-1.38)	8.0x10 <sup>-21</sup>	1.21 (1.18-1.24)	1.5x10 <sup>-45</sup>	2.2x10 <sup>-63</sup>
<i>PTHLH</i>	rs10771399	12	28046347	A/G	0.12	0.82 (0.77-0.87)	5.7x10 <sup>-10</sup>	0.86 (0.83-0.88)	3.2x10 <sup>-21</sup>	8.1x10 <sup>-31</sup>
12q24	rs1292011	12	114320905	A/G	0.42	0.91 (0.87-0.94)	9.5x10 <sup>-7</sup>	0.92 (0.90-0.94)	1.3x10 <sup>-16</sup>	8.9x10 <sup>-22</sup>



Locus	Original SNP <sup>1</sup>	Chr. <sup>2</sup>	Position <sup>3</sup>	Allele <sup>4</sup>	MAF <sup>5</sup>	Combined GWAS		iCOGS		Combined <i>P</i>
						Per allele OR <sup>6</sup> (95%CI)	Ptrend	Per allele OR <sup>6</sup> (95%CI)	Ptrend	
<i>RAD51L1</i>	rs999737	14	68104435	C/T	0.23	0.87 (0.83-0.91)	9.4x10 <sup>-9</sup>	0.92 (0.90-0.94)	6.7x10 <sup>-13</sup>	2.5x10 <sup>-19</sup>
<i>TOX3</i>	rs3803662	16	51143842	G/A	0.26	1.28 (1.23-1.34)	3.1x10 <sup>-30</sup>	1.24 (1.21-1.27)	2.2x10 <sup>-86</sup>	2.1x10 <sup>-114</sup>
<i>COX11</i>	rs6504950	17	50411470	G/A	0.28	0.91 (0.87-0.95)	9.4x10 <sup>-6</sup>	0.94 (0.92-0.96)	2.1x10 <sup>-9</sup>	2.3x10 <sup>-13</sup>
<i>MERIT40</i>	rs8170	19	17250704	G/A	0.19	1.03 (0.98-1.08)	0.22	1.04 (1.01-1.06)	0.0027	0.0012
<i>RALY</i> <sup>7</sup>	rs2284378	20	32051756	T/C	-	1.05 (1.01-1.10)	0.02	-	-	-
<i>NRIP1</i>	rs2823093	21	15442703	G/A	0.27	0.92 (0.88-0.96)	9.5x10 <sup>-5</sup>	0.92 (0.90-0.94)	1.5x10 <sup>-12</sup>	6.8x10 <sup>-16</sup>

<sup>1</sup> Published SNP showing the strongest association with breast cancer risk at that locus in European populations.

<sup>2</sup> Chromosome.

<sup>3</sup> Build 36 Position.

<sup>4</sup> Major/minor allele, based on the forward strand and minor allele frequency in Europeans.

<sup>5</sup> Mean Minor Allele Frequency over all European controls in iCOGS.

<sup>6</sup> Per allele odds ratio for the minor allele relative to the major allele.

<sup>7</sup> rs2284378 was not genotyped on iCOGS.

**Supplementary Table 5.** Multiple logistic regression analysis in iCOGS for four loci close to previously identified susceptibility loci, and four pairs of newly identified neighbouring loci within 1Mb of each other.

Region	First locus			Second Locus		
	SNP	OR (95%CI)	P-value	SNP	OR (95%CI)	P-value
2q35	rs4442975	0.87 (0.86-0.89)	$4.0 \times 10^{-44}$	rs16857609	1.08 (1.06-1.11)	$7.2 \times 10^{-13}$
9q31	rs865686	0.90 (0.88-0.91)	$1.7 \times 10^{-27}$	rs10759243	1.05 (1.03-1.08)	$9.4 \times 10^{-7}$
<i>FGFR2</i>	rs2981579	1.27 (1.25-1.30)	$1.0 \times 10^{-128}$	rs11199914	0.94 (0.92-0.96)	$2.4 \times 10^{-8}$
<i>RAD51L1</i>	rs999737	0.92 (0.90-0.95)	$3.5 \times 10^{-11}$	rs2588809	1.07 (1.05-1.10)	$1.2 \times 10^{-7}$
5q11.2	rs1353747	0.93 (0.90-0.97)	$7.7 \times 10^{-5}$	rs10472076	1.04 (1.02-1.06)	$4.5 \times 10^{-5}$
8q21.11	rs6472903	0.91 (0.88-0.93)	$7.6 \times 10^{-14}$	rs2943559	1.14 (1.10-1.18)	$3.9 \times 10^{-12}$
<i>DNAJC1</i>	rs11814448	1.22 (1.15-1.31)	$3.2 \times 10^{-9}$	rs7072776	1.05 (1.03-1.08)	$1.8 \times 10^{-6}$
18q11.2	rs527616	0.95 (0.93-0.97)	$4.7 \times 10^{-7}$	rs1436904	0.96 (0.94-0.98)	$9.8 \times 10^{-6}$

**Supplementary Table 6.** Genotype Specific Odds Ratios (ORs) in COGS replication for 41 SNPs showing evidence of association, and evidence for heterogeneity in the per-allele OR among studies.

Lead SNP	Chrom. <sup>1</sup>	Position <sup>2</sup>	Alleles <sup>3</sup>	Heterozygote OR (95%CI) <sup>4</sup>	Homozygote OR (95%CI) <sup>5</sup>	P (2df)	P for departure from log-additivity	Het P (Q) <sup>6</sup>	I <sup>2(7)</sup>
rs616488	1	10488802	T/C	0.97 (0.95-1.00)	0.86 (0.82-0.90)	2.0x10 <sup>-9</sup>	.0022	0.13	20.47
rs11552449	1	114249912	C/T	1.08 (1.04-1.11)	1.09 (1.01-1.19)	3.5x10 <sup>-6</sup>	0.24	1	0
rs4849887	2	120961592	C/T	0.90 (0.87-0.94)	0.85 (0.74-0.98)	3.7x10 <sup>-8</sup>	0.61	0.78	0
rs2016394	2	172681217	C/T	0.93 (0.90-0.96)	0.91 (0.87-0.94)	4.5x10 <sup>-7</sup>	0.096	0.21	14.83
rs1550623	2	173921140	T/C	0.94 (0.91-0.97)	0.90 (0.83-0.99)	6.1x10 <sup>-5</sup>	0.63	0.54	0
rs16857609	2	218004753	C/T	1.07 (1.04-1.10)	1.18 (1.12-1.25)	2.3x10 <sup>-11</sup>	0.31	0.16	17.97
rs6762644	3	4717276	A/G	1.07 (1.04-1.11)	1.13 (1.08-1.18)	2.2x10 <sup>-9</sup>	0.48	0.81	0
rs12493607	3	30657943	G/C	1.05 (1.02-1.08)	1.12 (1.07-1.17)	7.8x10 <sup>-7</sup>	0.50	0.03	31.01
rs9790517	4	106304227	C/T	1.06 (1.03-1.09)	1.10 (1.03-1.17)	8.1x10 <sup>-5</sup>	0.70	0.42	2.67
rs6828523	4	176083001	C/A	0.89 (0.86-0.92)	0.85 (0.75-0.95)	3.4x10 <sup>-12</sup>	0.29	0.54	0
rs10472076	5	58219818	T/C	1.04 (1.01-1.07)	1.11 (1.07-1.16)	5.0x10 <sup>-6</sup>	0.25	0.42	2.74
rs1353747	5	58373238	T/G	0.92 (0.89-0.96)	0.88 (0.76-1.01)	1.5x10 <sup>-5</sup>	0.70	0.58	0
rs1432679	5	158176661	A/G	1.08 (1.04-1.11)	1.15 (1.10-1.19)	1.8x10 <sup>-11</sup>	0.73	0.03	31
rs11242675	6	1263878	T/C	0.91 (0.88-0.94)	0.91 (0.87-0.95)	7.7x10 <sup>-10</sup>	0.0021	0.01	37.05

Lead SNP	Chrom. <sup>1</sup>	Position <sup>2</sup>	Alleles <sup>3</sup>	Heterozygote OR (95%CI) <sup>4</sup>	Homozygote OR (95%CI) <sup>5</sup>	P (2df)	P for departure from log- additivity	Het P (Q) <sup>6</sup>	I <sup>2</sup> (7)
rs204247	6	13830502	A/G	1.08 (1.05-1.12)	1.10 (1.05-1.14)	1.5x10 <sup>-7</sup>	0.016	0.37	5.69
rs720475	7	143705862	G/A	0.96 (0.93-0.98)	0.84 (0.80-0.89)	6.1x10 <sup>-9</sup>	0.033	0.37	5.46
rs9693444	8	29565535	C/A	1.07 (1.04-1.11)	1.15 (1.10-1.20)	2.2x10 <sup>-10</sup>	0.87	0.94	0
rs6472903	8	76392856	T/G	0.89 (0.86-0.91)	0.92 (0.85-1.00)	3.2x10 <sup>-14</sup>	0.00096	0.64	0
rs2943559	8	76580492	A/G	1.12 (1.08-1.17)	1.35 (1.14-1.61)	3.5x10 <sup>-10</sup>	0.44	0.26	11.89
rs11780156	8	129263823	C/T	1.07 (1.04-1.11)	1.13 (1.04-1.22)	3.0x10 <sup>-6</sup>	0.66	0.74	0
rs10759243	9	109345936	C/A	1.05 (1.02-1.08)	1.12 (1.07-1.18)	2.4x10 <sup>-6</sup>	0.69	0.93	0
rs7072776	10	22072948	G/A	1.07 (1.04-1.10)	1.13 (1.08-1.19)	1.1x10 <sup>-8</sup>	0.66	0.33	7.97
rs11814448	10	22355849	A/C	1.26 (1.19-1.35)	1.51 (0.89-2.54)	2.6x10 <sup>-11</sup>	0.83	0.55	0
rs7904519	10	114763917	A/G	1.05 (1.02-1.09)	1.11 (1.08-1.16)	1.1x10 <sup>-7</sup>	0.80	0.57	0
rs11199914	10	123083891	C/T	0.95 (0.92-0.97)	0.91 (0.87-0.95)	7.8x10 <sup>-6</sup>	0.58	0.45	0.98
rs3903072	11	65339642	C/A	0.95 (0.92-0.98)	0.90 (0.86-0.93)	1.4x10 <sup>-7</sup>	0.96	0.65	0
rs11820646	11	128966381	C/T	0.95 (0.92-0.98)	0.90 (0.87-0.94)	2.0x10 <sup>-6</sup>	0.77	0.79	0
rs12422552	12	14305198	G/C	1.04 (1.01-1.07)	1.12 (1.06-1.19)	6.8x10 <sup>-5</sup>	0.19	0.06	27.04
rs17356907	12	94551890	A/G	0.91 (0.89-0.94)	0.83 (0.79-0.87)	1.4x10 <sup>-16</sup>	0.86	0.20	15.68
rs11571833	13	31870626	A/T	1.25	5.78	1.2x10 <sup>-5</sup>	0.16	0.19	16

Lead SNP	Chrom. <sup>1</sup>	Position <sup>2</sup>	Alleles <sup>3</sup>	Heterozygote OR (95%CI) <sup>4</sup>	Homozygote OR (95%CI) <sup>5</sup>	P (2df)	P for departure from log-additivity	Het P (Q) <sup>6</sup>	I <sup>2(7)</sup>
				(1.13-1.38)	(0.70-47.5)				
rs2236007	14	36202520	G/A	0.92 (0.89-0.95)	0.88 (0.82-0.94)	2.3x10 <sup>-9</sup>	0.36	0.63	0
rs2588809	14	67730181	C/T	1.08 (1.05-1.11)	1.19 (1.09-1.29)	1.6x10 <sup>-8</sup>	0.66	0.41	3.46
rs941764	14	90910822	A/G	1.07 (1.04-1.10)	1.13 (1.08-1.18)	1.7x10 <sup>-8</sup>	0.82	0.76	0
rs17817449	16	52370868	T/G	0.95 (0.92-0.98)	0.86 (0.83-0.90)	4.2x10 <sup>-12</sup>	0.15	0.87	0
rs13329835	16	79208306	A/G	1.09 (1.06-1.12)	1.15 (1.08-1.22)	3.7x10 <sup>-10</sup>	0.47	0.35	6.52
rs527616	18	22591422	C/G	0.96 (0.93-0.99)	0.90 (0.86-0.94)	1.7x10 <sup>-6</sup>	0.50	0.56	0
rs1436904	18	22824665	T/G	0.97 (0.94-0.99)	0.91 (0.87-0.95)	2.7x10 <sup>-5</sup>	0.38	0.58	0
rs4808801	19	18432141	A/G	0.94 (0.91-0.97)	0.85 (0.81-0.89)	2.0x10 <sup>-12</sup>	0.28	0.07	25.89
rs3760982	19	48978353	G/A	1.05 (1.02-1.08)	1.12 (1.07-1.16)	1.5x10 <sup>-7</sup>	0.57	0.94	0
rs132390	22	27951477	T/C	1.12 (1.06-1.18)	1.37 (0.94-1.99)	3.1x10 <sup>-5</sup>	0.66	0.08	24.82
rs6001930	22	39206180	T/C	1.13 (1.09-1.17)	1.20 (1.07-1.36)	1.3x10 <sup>-12</sup>	0.41	0.64	0

<sup>1</sup>Chromosome.

<sup>2</sup>Build 36 Position.

<sup>3</sup>Major/minor allele, based on the forward strand and minor allele frequency in Europeans.

<sup>4</sup>OR for heterozygotes relative to major allele homozygotes.

<sup>5</sup>OR for homozygotes relative to minor allele homozygotes

<sup>6</sup>P-value for heterogeneity in the per-allele ORs among studies (Q statistic)

<sup>7</sup>I<sup>2</sup> statistic for heterogeneity in the per-allele ORs among studies

**Supplementary Table 7.** Associations by disease subtype in COGS replication, for 41 SNPs showing overall evidence of association.

**Supplementary Table 7a.** Per-allele ORs for ER- vs. ER+ disease (based on 7,465 ER-negative cases and 27,074 ER-positive cases).

Lead SNP	Chrom.	Position	ER- OR (95%CI)	ER- P	ER+ OR (95%CI)	ER+ P	ER+ vs. ER- P- value
rs616488	1	10488802	0.91 (0.88-0.95)	$5.4 \times 10^{-6}$	0.96 (0.94-0.98)	0.0013	0.073
rs11552449	1	114249912	1.04 (0.99-1.10)	0.10	1.08 (1.05-1.11)	$9.4 \times 10^{-7}$	0.11
rs4849887	2	120961592	0.91 (0.85-0.97)	0.0041	0.91 (0.88-0.95)	$2.1 \times 10^{-6}$	0.97
rs2016394	2	172681217	1.00 (0.96-1.03)	0.8	0.94 (0.92-0.96)	$1.1 \times 10^{-8}$	0.0028
rs1550623	2	173921140	0.94 (0.90-1.00)	0.032	0.94 (0.92-0.98)	0.00036	0.87
rs16857609	2	218004753	1.08 (1.03-1.12)	0.00051	1.08 (1.05-1.11)	$3.3 \times 10^{-9}$	0.86
rs6762644	3	4717276	1.02 (0.98-1.06)	0.28	1.07 (1.04-1.09)	$1.4 \times 10^{-8}$	0.017
rs12493607	3	30657943	1.02 (0.98-1.06)	0.40	1.07 (1.04-1.09)	$1.0 \times 10^{-7}$	0.023
rs9790517	4	106304227	1.03 (0.98-1.08)	0.21	1.06 (1.03-1.09)	0.000033	0.41
rs6828523	4	176083001	1.01 (0.96-1.07)	0.66	0.87 (0.84-0.90)	$2.9 \times 10^{-14}$	$1.2 \times 10^{-7}$
rs10472076	5	58219818	1.05 (1.01-1.09)	0.01	1.03 (1.01-1.06)	0.002	0.32
rs1353747	5	58373238	0.92 (0.86-0.98)	0.011	0.93 (0.90-0.97)	0.00068	0.46
rs1432679	5	158176661	1.09 (1.05-1.13)	$9.0 \times 10^{-6}$	1.07 (1.05-1.09)	$6.2 \times 10^{-9}$	0.83
rs11242675	6	1263878	0.94 (0.90-0.97)	0.0011	0.94 (0.92-0.97)	$1.6 \times 10^{-6}$	0.29

Lead SNP	Chrom.	Position	ER- OR (95%CI)	ER- P	ER+ OR (95%CI)	ER+ P	ER+ vs. ER- P- value
rs204247	6	13830502	1.00 (0.97-1.04)	0.81	1.06 (1.04-1.09)	$9.0 \times 10^{-8}$	0.017
rs720475	7	143705862	0.99 (0.95-1.03)	0.55	0.93 (0.90-0.95)	$2.9 \times 10^{-8}$	0.026
rs9693444	8	29565535	1.09 (1.05-1.13)	0.000026	1.07 (1.05-1.10)	$6.8 \times 10^{-9}$	0.54
rs6472903	8	76392856	0.94 (0.89-0.98)	0.00090	0.91 (0.88-0.94)	$9.7 \times 10^{-10}$	0.32
rs2943559	8	76580492	1.07 (1.00-1.15)	0.044	1.13 (1.09-1.18)	$7.9 \times 10^{-9}$	0.24
rs11780156	8	129263823	1.06 (1.00-1.11)	0.034	1.08 (1.04-1.11)	$1.9 \times 10^{-6}$	0.11
rs10759243	9	109345936	1.01 (0.97-1.05)	0.73	1.08 (1.05-1.11)	$6.0 \times 10^{-10}$	0.0017
rs7072776	10	22072948	0.94 (0.90-0.98)	0.005	1.09 (1.06-1.12)	$2.5 \times 10^{-11}$	$3.1 \times 10^{-10}$
rs11814448	10	22355849	1.19 (1.05-1.35)	0.0076	1.25 (1.16-1.35)	$8.6 \times 10^{-9}$	0.21
rs7904519	10	114763917	1.05 (1.01-1.09)	0.0068	1.05 (1.02-1.07)	0.000080	0.62
rs11199914	10	123083891	1.02 (0.98-1.06)	0.30	0.94 (0.91-0.96)	$9.1 \times 10^{-8}$	0.000038
rs3903072	11	65339642	0.97 (0.94-1.01)	0.14	0.94 (0.92-0.96)	$4.7 \times 10^{-7}$	0.063
rs11820646	11	128966381	0.96 (0.92-0.99)	0.024	0.95 (0.93-0.97)	$3.6 \times 10^{-6}$	0.66
rs12422552	12	14305198	1.04 (1.00-1.09)	0.050	1.04 (1.02-1.07)	0.0012	0.81
rs17356907	12	94551890	0.94 (0.91-0.98)	0.0053	0.91 (0.88-0.93)	$1.2 \times 10^{-14}$	0.24
rs11571833	13	31870626	1.43 (1.20-1.71)	0.000088	1.26 (1.12-1.41)	0.00014	0.15
rs2236007	14	36202520	0.96	0.081	0.91	$1.9 \times 10^{-10}$	0.015



Lead SNP	Chrom.	Position	ER- OR (95%CI)	ER- P	ER+ OR (95%CI)	ER+ P	ER+ vs. ER- P- value
			(0.92-1.01)		(0.89-0.94)		
rs2588809	14	67730181	1.02 (0.97-1.07)	0.49	1.10 (1.06-1.13)	$5.7 \times 10^{-9}$	0.011
rs941764	14	90910822	1.03 (0.99-1.07)	0.1	1.07 (1.05-1.10)	$4.8 \times 10^{-9}$	0.15
rs17817449	16	52370868	0.91 (0.87-0.94)	$4.1 \times 10^{-7}$	0.94 (0.91-0.96)	$1.2 \times 10^{-8}$	0.039
rs13329835	16	79208306	1.02 (0.98-1.07)	0.37	1.09 (1.06-1.12)	$3.4 \times 10^{-10}$	0.017
rs527616	18	22591422	0.98 (0.94-1.02)	0.24	0.95 (0.93-0.97)	0.000040	0.31
rs1436904	18	22824665	1.00 (0.96-1.04)	0.97	0.93 (0.92-0.96)	$7.3 \times 10^{-8}$	0.0002
rs4808801	19	18432141	0.92 (0.88-0.96)	0.000030	0.93 (0.91-0.95)	$1.4 \times 10^{-9}$	0.77
rs3760982	19	48978353	1.04 (1.00-1.08)	0.029	1.06 (1.04-1.08)	$3.3 \times 10^{-7}$	0.54
rs132390	22	27951477	1.08 (0.98-1.19)	0.11	1.13 (1.07-1.20)	0.000042	0.41
rs6001930	22	39206180	1.10 (1.04-1.17)	0.0011	1.12 (1.08-1.16)	$6.1 \times 10^{-10}$	0.52

**Supplementary Table 7b.** Per-allele ORs for DCIS vs. invasive disease (based on 2,335 DCIS and 42,118 invasive cases).

Lead SNP	Chrom.	Position	DCIS OR (95%CI)	DCIS P	Invasive OR (95%CI)	Invasive P	DCIS vs. invasive P-value
rs616488	1	10488802	0.96 (0.90-1.03)	0.27	0.94 (0.92-0.96)	$1.7 \times 10^{-8}$	0.78
rs11552449	1	114249912	1.04 (0.96-1.13)	0.31	1.07 (1.04-1.10)	$7.4 \times 10^{-7}$	0.64
rs4849887	2	120961592	0.91 (0.82-1.01)	0.076	0.91 (0.88-0.94)	$7.6 \times 10^{-9}$	0.78
rs2016394	2	172681217	0.97 (0.91-1.03)	0.33	0.95 (0.93-0.97)	$7.3 \times 10^{-8}$	0.29
rs1550623	2	173921140	0.96 (0.89-1.05)	0.39	0.94 (0.92-0.97)	$1.0 \times 10^{-5}$	0.52
rs16857609	2	218004753	1.10 (1.03-1.18)	0.0048	1.08 (1.06-1.10)	$1.2 \times 10^{-11}$	0.66
rs6762644	3	4717276	1.09 (1.02-1.16)	0.0076	1.06 (1.04-1.09)	$1.2 \times 10^{-9}$	0.34
rs12493607	3	30657943	0.98 (0.92-1.04)	0.51	1.06 (1.04-1.08)	$3.4 \times 10^{-8}$	0.0087
rs9790517	4	106304227	1.02 (0.95-1.10)	0.59	1.05 (1.03-1.08)	$1.8 \times 10^{-5}$	0.36
rs6828523	4	176083001	0.88 (0.80-0.97)	0.013	0.90 (0.87-0.92)	$2.6 \times 10^{-12}$	0.74
rs10472076	5	58219818	1.08 (1.02-1.15)	0.01	1.05 (1.03-1.07)	$4.0 \times 10^{-6}$	0.21
rs1353747	5	58373238	0.88 (0.79-0.99)	0.027	0.92 (0.89-0.96)	$5.3 \times 10^{-6}$	0.26
rs1432679	5	158176661	1.05 (0.98-1.11)	0.13	1.07 (1.05-1.09)	$2.7 \times 10^{-12}$	0.94
rs11242675	6	1263878	0.92 (0.86-0.98)	0.010	0.94 (0.92-0.96)	$2.0 \times 10^{-8}$	0.75
rs204247	6	13830502	1.04 (0.98-1.10)	0.25	1.05 (1.03-1.07)	$9.0 \times 10^{-7}$	0.71

Lead SNP	Chrom.	Position	DCIS OR (95%CI)	DCIS P	Invasive OR (95%CI)	Invasive P	DCIS vs. invasive P-value
rs720475	7	143705862	0.93 (0.86-0.99)	0.032	0.94 (0.92-0.96)	$7.4 \times 10^{-8}$	0.90
rs9693444	8	29565535	1.08 (1.02-1.15)	0.014	1.07 (1.05-1.09)	$2.7 \times 10^{-10}$	0.55
rs6472903	8	76392856	0.91 (0.84-0.99)	0.026	0.91 (0.89-0.94)	$5.7 \times 10^{-12}$	0.81
rs2943559	8	76580492	1.14 (1.01-1.27)	0.03	1.13 (1.09-1.18)	$3.6 \times 10^{-11}$	0.99
rs11780156	8	129263823	1.09 (1.01-1.19)	0.030	1.07 (1.04-1.09)	$1.8 \times 10^{-6}$	0.74
rs10759243	9	109345936	1.02 (0.96-1.09)	0.52	1.06 (1.04-1.08)	$3.3 \times 10^{-7}$	0.27
rs7072776	10	22072948	1.00 (0.94-1.07)	0.91	1.07 (1.05-1.10)	$3.5 \times 10^{-10}$	0.03
rs11814448	10	22355849	1.31 (1.09-1.59)	0.0052	1.26 (1.17-1.34)	$2.7 \times 10^{-11}$	0.67
rs7904519	10	114763917	1.04 (0.98-1.11)	0.16	1.06 (1.04-1.08)	$2.8 \times 10^{-8}$	0.77
rs11199914	10	123083891	0.97 (0.90-1.03)	0.29	0.95 (0.93-0.97)	$8.3 \times 10^{-6}$	0.60
rs3903072	11	65339642	1.01 (0.95-1.07)	0.79	0.94 (0.92-0.96)	$1.9 \times 10^{-9}$	0.026
rs11820646	11	128966381	0.95 (0.89-1.01)	0.090	0.95 (0.93-0.97)	$5.2 \times 10^{-7}$	0.98
rs12422552	12	14305198	1.11 (1.04-1.19)	0.0030	1.04 (1.02-1.07)	$1.9 \times 10^{-4}$	0.13
rs17356907	12	94551890	0.91 (0.85-0.97)	0.0066	0.91 (0.89-0.93)	$2.2 \times 10^{-16}$	0.85
rs11571833	13	31870626	1.45 (1.09-1.94)	0.012	1.25 (1.13-1.39)	$1.6 \times 10^{-5}$	0.48
rs2236007	14	36202520	0.93 (0.86-1.00)	0.048	0.93 (0.91-0.95)	$1.1 \times 10^{-9}$	0.81
rs2588809	14	67730181	1.10 (1.01-1.19)	0.023	1.08 (1.05-1.11)	$7.9 \times 10^{-9}$	0.67

Lead SNP	Chrom.	Position	DCIS OR (95%CI)	DCIS P	Invasive OR (95%CI)	Invasive P	DCIS vs. invasive P-value
rs941764	14	90910822	1.06 (1.00-1.13)	0.063	1.06 (1.04-1.09)	$4.6 \times 10^{-9}$	0.90
rs17817449	16	52370868	0.90 (0.85-0.96)	0.0015	0.93 (0.92-0.95)	$3.5 \times 10^{-11}$	0.24
rs13329835	16	79208306	1.08 (1.01-1.16)	0.028	1.08 (1.05-1.10)	$2.3 \times 10^{-10}$	1.00
rs527616	18	22591422	0.96 (0.91-1.03)	0.25	0.95 (0.93-0.97)	$2.9 \times 10^{-7}$	0.69
rs1436904	18	22824665	0.98 (0.93-1.04)	0.66	0.95 (0.93-0.97)	$4.0 \times 10^{-6}$	0.16
rs4808801	19	18432141	0.88 (0.82-0.94)	$7.7 \times 10^{-5}$	0.93 (0.91-0.95)	$4.5 \times 10^{-12}$	0.12
rs3760982	19	48978353	1.01 (0.95-1.08)	0.66	1.06 (1.04-1.08)	$1.6 \times 10^{-8}$	0.13
rs132390	22	27951477	1.05 (0.90-1.23)	0.56	1.13 (1.07-1.19)	$4.0 \times 10^{-6}$	0.44
rs6001930	22	39206180	1.18 (1.08-1.29)	0.00036	1.12 (1.08-1.15)	$3.7 \times 10^{-12}$	0.21

**Supplementary Table 7c.** Per-allele ORs by age at diagnosis.

Lead SNP	Chrom.	Position	Per-allele OR (95%CI) by age at diagnosis				P-value for trend
			<40	40-49	50-59	60+	
rs616488	1	10488802	0.91 (0.87-0.96)	0.90 (0.87-0.94)	0.94 (0.92-0.97)	0.97 (0.94-1.00)	0.32
rs11552449	1	114249912	1.09 (1.02-1.17)	1.08 (1.04-1.13)	1.05 (1.01-1.09)	1.07 (1.03-1.11)	0.30
rs4849887	2	120961592	0.88 (0.80-0.96)	0.90 (0.85-0.95)	0.91 (0.87-0.96)	0.92 (0.88-0.96)	0.66
rs2016394	2	172681217	0.93 (0.88-0.98)	0.95 (0.92-0.98)	0.95 (0.92-0.98)	0.95 (0.92-0.97)	0.54
rs1550623	2	173921140	0.86 (0.80-0.93)	0.92 (0.88-0.97)	0.93 (0.90-0.97)	0.97 (0.94-1.01)	0.06
rs16857609	2	218004753	1.09 (1.03-1.15)	1.09 (1.05-1.14)	1.08 (1.05-1.11)	1.07 (1.04-1.10)	0.02
rs6762644	3	4717276	1.15 (1.09-1.21)	1.07 (1.03-1.10)	1.07 (1.04-1.10)	1.07 (1.04-1.10)	0.19
rs12493607	3	30657943	1.04 (0.99-1.10)	1.05 (1.01-1.09)	1.07 (1.04-1.11)	1.04 (1.02-1.07)	0.29
rs9790517	4	106304227	1.05 (0.99-1.12)	1.07 (1.03-1.11)	1.05 (1.02-1.09)	1.04 (1.00-1.07)	0.12
rs6828523	4	176083001	0.94 (0.87-1.02)	0.87 (0.83-0.92)	0.90 (0.86-0.94)	0.89 (0.86-0.93)	0.56
rs10472076	5	58219818	1.05 (0.99-1.11)	1.03 (0.99-1.07)	1.05 (1.02-1.08)	1.05 (1.02-1.08)	0.12
rs1353747	5	58373238	0.91 (0.84-1.00)	0.93 (0.88-0.98)	0.92 (0.88-0.97)	0.92 (0.88-0.96)	0.43
rs1432679	5	158176661	1.11 (1.06-1.17)	1.07 (1.03-1.10)	1.08 (1.05-1.12)	1.06 (1.03-1.09)	0.11
rs11242675	6	1263878	0.96 (0.91-1.01)	0.94 (0.91-0.98)	0.93 (0.90-0.95)	0.95 (0.93-0.98)	0.92
rs204247	6	13830502	1.06 (1.01-1.12)	1.06 (1.02-1.09)	1.06 (1.03-1.08)	1.04 (1.02-1.07)	0.23

Lead SNP	Chrom.	Position	Per-allele OR (95%CI) by age at diagnosis				P-value for trend
			<40	40-49	50-59	60+	
rs720475	7	143705862	0.89 (0.83-0.94)	0.93 (0.89-0.96)	0.94 (0.91-0.97)	0.95 (0.92-0.98)	0.25
rs9693444	8	29565535	1.06 (1.01-1.12)	1.04 (1.00-1.08)	1.08 (1.05-1.12)	1.08 (1.05-1.11)	0.06
rs6472903	8	76392856	0.86 (0.80-0.92)	0.89 (0.85-0.93)	0.91 (0.88-0.95)	0.94 (0.91-0.98)	0.14
rs2943559	8	76580492	1.15 (1.05-1.26)	1.15 (1.08-1.22)	1.10 (1.05-1.16)	1.13 (1.07-1.18)	0.88
rs11780156	8	129263823	1.09 (1.02-1.17)	1.07 (1.02-1.12)	1.08 (1.05-1.12)	1.05 (1.02-1.09)	0.59
rs10759243	9	109345936	1.04 (0.99-1.10)	1.07 (1.03-1.11)	1.06 (1.03-1.09)	1.05 (1.02-1.08)	0.68
rs7072776	10	22072948	1.04 (0.99-1.10)	1.08 (1.04-1.12)	1.08 (1.05-1.11)	1.06 (1.03-1.09)	0.99
rs11814448	10	22355849	1.23 (1.04-1.45)	1.19 (1.06-1.33)	1.24 (1.13-1.36)	1.30 (1.19-1.42)	0.58
rs7904519	10	114763917	1.12 (1.06-1.17)	1.07 (1.03-1.10)	1.06 (1.03-1.09)	1.04 (1.01-1.07)	0.63
rs11199914	10	123083891	0.96 (0.91-1.01)	0.93 (0.90-0.97)	0.95 (0.92-0.98)	0.97 (0.94-0.99)	0.05
rs3903072	11	65339642	0.92 (0.87-0.97)	0.91 (0.88-0.94)	0.96 (0.93-0.98)	0.96 (0.93-0.99)	0.41
rs11820646	11	128966381	0.89 (0.85-0.94)	0.93 (0.90-0.96)	0.96 (0.93-0.99)	0.96 (0.93-0.99)	0.12
rs12422552	12	14305198	1.08 (1.02-1.14)	1.03 (1.00-1.07)	1.05 (1.02-1.08)	1.05 (1.02-1.08)	0.09
rs17356907	12	94551890	0.93 (0.88-0.98)	0.91 (0.88-0.94)	0.91 (0.88-0.94)	0.91 (0.89-0.94)	0.53
rs11571833	13	31870626	1.51 (1.20-1.92)	1.30 (1.10-1.53)	1.27 (1.11-1.47)	1.21 (1.06-1.38)	0.34
rs2236007	14	36202520	0.96 (0.90-1.02)	0.93 (0.89-0.97)	0.92 (0.89-0.96)	0.93 (0.90-0.96)	0.33
rs2588809	14	67730181	1.12	1.12	1.11	1.03	0.001

Lead SNP	Chrom.	Position	Per-allele OR (95%CI) by age at diagnosis				P-value for trend
			<40	40-49	50-59	60+	
			(1.05-1.19)	(1.07-1.17)	(1.07-1.15)	(1.00-1.07)	
rs941764	14	90910822	1.08 (1.02-1.13)	1.10 (1.06-1.13)	1.08 (1.05-1.11)	1.03 (1.00-1.06)	0.007
rs17817449	16	52370868	0.93 (0.88-0.98)	0.91 (0.88-0.94)	0.93 (0.90-0.95)	0.95 (0.92-0.97)	0.27
rs13329835	16	79208306	1.07 (1.00-1.13)	1.07 (1.03-1.11)	1.10 (1.06-1.13)	1.07 (1.04-1.11)	0.73
rs527616	18	22591422	0.94 (0.89-0.99)	0.93 (0.90-0.96)	0.95 (0.93-0.98)	0.96 (0.94-0.99)	0.51
rs1436904	18	22824665	1.01 (0.96-1.07)	0.97 (0.93-1.00)	0.94 (0.91-0.96)	0.95 (0.93-0.98)	0.12
rs4808801	19	18432141	0.93 (0.88-0.98)	0.91 (0.88-0.95)	0.93 (0.90-0.96)	0.93 (0.90-0.95)	0.18
rs3760982	19	48978353	1.08 (1.03-1.14)	1.04 (1.01-1.07)	1.08 (1.05-1.11)	1.04 (1.02-1.07)	0.90
rs132390	22	27951477	1.19 (1.05-1.35)	1.13 (1.04-1.24)	1.14 (1.07-1.23)	1.08 (1.01-1.16)	0.17
rs6001930	22	39206180	1.16 (1.07-1.26)	1.10 (1.04-1.16)	1.09 (1.04-1.14)	1.14 (1.09-1.19)	0.38

**Supplementary Table 7d.** Per-allele ORs by Family History, based on 8,246 cases with an affected first-degree and 21,526 cases without an affected first-degree relative.

SNP	Chromosome	Position	FH+ OR <sup>1</sup> (95% CI)	FH+ P	FH- OR <sup>2</sup> (95%CI)	FH- P	FH + vs FH-
rs616488	1	10488802	0.94 (0.90-0.98)	0.0013	0.95 (0.92-0.98)	0.00024	0.37
rs11552449	1	114249912	1.09 (1.04-1.15)	0.00035	1.06 (1.03-1.10)	0.00049	0.11
rs4849887	2	120961592	0.89 (0.83-0.95)	0.00024	0.91 (0.87-0.96)	5.5x10 <sup>-5</sup>	0.39
rs2016394	2	172681217	0.91 (0.87-0.94)	1.8E-07	0.95 (0.93-0.98)	0.00017	0.064
rs1550623	2	173921140	0.90 (0.86-0.94)	8.7E-05	0.94 (0.91-0.98)	0.0011	0.17
rs16857609	2	218004753	1.11 (1.06-1.15)	1.6E-06	1.08 (1.05-1.11)	7.3x10 <sup>-8</sup>	0.93
rs6762644	3	4717276	1.06 (1.02-1.10)	0.0022	1.06 (1.03-1.09)	1.1x10 <sup>-5</sup>	0.87
rs12493607	3	30657943	1.08 (1.04-1.13)	2.9x10 <sup>-5</sup>	1.05 (1.02-1.08)	0.00054	0.14
rs9790517	4	106304227	1.04 (0.99-1.09)	0.091	1.04 (1.01-1.07)	0.0082	0.63
rs6828523	4	176083001	0.85 (0.80-0.90)	5.7x10 <sup>-8</sup>	0.89 (0.86-0.93)	2.6x10 <sup>-8</sup>	0.48
rs10472076	5	58219818	1.07 (1.03-1.11)	0.0005	1.05 (1.03-1.08)	7.2x10 <sup>-5</sup>	0.77
rs1353747	5	58373238	0.92 (0.87-0.98)	0.013	0.90 (0.86-0.94)	4.2x10 <sup>-6</sup>	0.82
rs1432679	5	158176661	1.12 (1.08-1.16)	2.1x10 <sup>-9</sup>	1.06 (1.03-1.09)	9.3x10 <sup>-6</sup>	0.0064
rs11242675	6	1263878	0.96	0.028	0.96	0.0036	0.54



SNP	Chromosome	Position	FH+ OR <sup>1</sup> (95% CI)	FH+ P	FH- OR <sup>2</sup> (95%CI)	FH- P	FH + vs FH-
			(0.92-1)		(0.94-0.99)		
rs204247	6	13830502	1.06 (1.02-1.10)	0.0035	1.04 (1.02-1.07)	0.0011	0.77
rs720475	7	143705862	0.92 (0.88-0.95)	3.3x10 <sup>-5</sup>	0.95 (0.92-0.97)	0.00020	0.089
rs9693444	8	29565535	1.07 (1.03-1.12)	0.00036	1.08 (1.05-1.12)	1.1x10 <sup>-8</sup>	0.64
rs6472903	8	76392856	0.91 (0.86-0.95)	9.6x10 <sup>-5</sup>	0.92 (0.89-0.95)	2.5x10 <sup>-6</sup>	0.62
rs2943559	8	76580492	1.22 (1.14-1.30)	3.1x10 <sup>-9</sup>	1.11 (1.06-1.17)	1.7x10 <sup>-5</sup>	0.006
rs11780156	8	129263823	1.07 (1.02-1.12)	0.0044	1.07 (1.03-1.11)	0.00011	0.75
rs10759243	9	109345936	1.06 (1.02-1.10)	0.0031	1.06 (1.02-1.09)	0.00015	0.48
rs7072776	10	22072948	1.07 (1.03-1.11)	0.001	1.07 (1.04-1.10)	2.8x10 <sup>-6</sup>	0.18
rs11814448	10	22355849	1.27 (1.13-1.43)	9.3x10 <sup>-5</sup>	1.30 (1.19-1.42)	3.8x10 <sup>-9</sup>	0.54
rs7904519	10	114763917	1.06 (1.03-1.10)	0.00067	1.06 (1.03-1.08)	2.8x10 <sup>-5</sup>	0.76
rs11199914	10	123083891	0.94 (0.91-0.98)	0.0036	0.95 (0.92-0.98)	0.00026	0.19
rs3903072	11	65339642	0.92 (0.83-0.95)	2.4x10 <sup>-6</sup>	0.96 (0.94-0.98)	0.0016	0.032
rs11820646	11	128966381	0.95 (0.92-0.99)	0.0094	0.94 (0.92-0.97)	1.3x10 <sup>-5</sup>	0.20
rs12422552	12	14305198	1.07 (1.03-1.12)	0.00078	1.06 (1.03-1.09)	5.8x10 <sup>-5</sup>	0.84
rs17356907	12	94551890	0.89 (0.85-0.92)	5.1x10 <sup>-9</sup>	0.93 (0.9-0.95)	6.6x10 <sup>-8</sup>	0.15
rs11571833	13	31870626	1.54 (1.3-1.83)	7.2x10 <sup>-7</sup>	1.25 (1.10-1.43)	0.00082	0.026

SNP	Chromosome	Position	FH+ OR <sup>1</sup> (95% CI)	FH+ P	FH- OR <sup>2</sup> (95%CI)	FH- P	FH + vs FH-
rs2236007	14	36202520	0.89 (0.85-0.93)	1.0x10 <sup>-6</sup>	0.93 (0.91-0.97)	8.0x10 <sup>-5</sup>	0.16
rs2588809	14	67730181	1.11 (1.06-1.17)	1.9x10 <sup>-5</sup>	1.10 (1.06-1.14)	1.1x10 <sup>-7</sup>	0.72
rs941764	14	90910822	1.06 (1.02-1.10)	0.0056	1.07 (1.03-1.10)	4.4x10 <sup>-6</sup>	0.98
rs17817449	16	52370868	0.93 (0.90-0.97)	0.00013	0.93 (0.91-0.96)	1.6x10 <sup>-7</sup>	0.64
rs13329835	16	79208306	1.12 (1.07-1.17)	1.4x10 <sup>-7</sup>	1.06 (1.03-1.10)	0.00012	0.037
rs527616	18	22591422	0.94 (0.90-0.97)	0.00056	0.96 (0.94-0.99)	0.0045	0.87
rs1436904	18	22824665	0.97 (0.93-1.00)	0.09	0.96 (0.93-0.98)	0.001	0.89
rs4808801	19	18432141	0.89 (0.86-0.93)	6.6x10 <sup>-9</sup>	0.92 (0.90-0.95)	5.9x10 <sup>-9</sup>	0.59
rs3760982	19	48978353	1.06 (1.02-1.10)	0.0033	1.06 (1.03-1.09)	6.9x10 <sup>-6</sup>	0.90
rs132390	22	27951477	1.26 (1.15-1.38)	9.8x10 <sup>-7</sup>	1.09 (1.01-1.16)	0.019	0.011
rs6001930	22	39206180	1.17 (1.11-1.24)	3.9x10 <sup>-8</sup>	1.13 (1.09-1.18)	3.2x10 <sup>-9</sup>	0.22

<sup>1</sup>Per-allele OR for cases with a positive first-degree family history

<sup>2</sup>Per-allele OR for cases without a positive first-degree family history

**Supplementary Table 8a.** *cis* eQTL analysis. Expression in breast tumor (n=473) and normal tissue (n=61) from TCGA. Genes within 50kb of the lead SNP, with nominal association  $P < .01$ .

Lead SNP	Gene	Proxy SNP	$r^2$	Tumor Tissue		Normal Tissue	
				<i>P</i> -value	<i>P</i> -value adjusted model*	<i>P</i> -value	<i>P</i> -value adjusted model
rs616488	<i>PEX14</i>	rs616402	0.66	$3.8 \times 10^{-12}$	0.0071	0.00021	0.102
rs11552449	<i>PTPN22</i>	rs1217396	0.70	0.021	0.0055	0.16	0.63
rs11552449	<i>DCLRE1B</i>	rs1217396	0.70	0.0123	0.0067	0.89	0.60
rs3903072	<i>CFL1</i>	n/a**	n/a	0.022	0.73	0.054	0.0014

\* Association adjusted for top-eQTL SNP

\*\* rs3903072 is represented directly on the microarray

**Supplementary Table 8b.** Genes tested for *cis* eQTL analysis.

SNP	# Genes	Genes
rs616488	2	<i>DFFA,PEX14</i>
rs11552449	5	<i>HIPK1,AP4B1,PTPN22,DCLRE1B,BCL2L15</i>
rs4849887	1	<i>LOC84931</i>
rs2016394	0	
rs1550623	2	<i>RPS2P18,CDCA7</i>
rs16857609	0	
rs6762644	1	<i>ITPR1</i>
rs12493607	1	<i>TGFBR2</i>
rs9790517	1	<i>TET2</i>
rs6828523	1	<i>ADAM29</i>
rs10472076	1	<i>RAB3C</i>
rs1353747	0	
rs1432679	1	<i>EBF1</i>
rs11242675	1	<i>FOXQ1</i>
rs204247	1	<i>RANBP9</i>
rs720475	1	<i>ARHGEF5</i>
rs9693444	1	<i>RPL17P33</i>
rs6472903	0	
rs2943559	1	<i>HNF4G</i>
rs11780156	0	
rs10759243	0	
rs7072776	2	<i>DNAJC1,MLLT10</i>
rs11814448	1	<i>DNAJC1</i>
rs7904519	1	<i>TCF7L2</i>
rs11199914	0	
rs3903072	5	<i>OVOL1,SNX32,CFL1,MUS81,AP5B1</i>
rs11820646	0	
rs12422552	0	

SNP	# Genes	Genes
rs17356907	1	<i>NTN4</i>
rs11571833	0	
rs2236007	2	<i>PAX9,SLC25A21</i>
rs2588809	1	<i>RAD51B</i>
rs941764	1	<i>CCDC88C</i>
rs17817449	1	<i>FTO</i>
rs13329835	1	<i>CDYL2</i>
rs527616	0	
rs1436904	1	<i>CHST9</i>
rs4808801	3	<i>ELL,ISYNA1,SSBP4</i>
rs3760982	4	<i>KCNN4,ZNF283,SMG9,LYPD5</i>
rs132390	0	
rs6001930	1	<i>MKL1</i>
rs616488	2	
rs11552449	5	

**Supplementary Table 8c.** Expression in lymphocytes in 109 samples from individuals of European ancestry from Hapmap CEU. Genes within 500kb of the lead SNP showing associations between expression and genotype at  $P < 0.1$  (from 94 genes expressed in lymphocytes).

SNP	Chromosome	Position	Gene	<i>P-value</i>
rs616488	1	10488802	<i>KIF1B</i>	0.09
rs10759243	9	109345936	<i>RAD23B</i>	0.03
rs4808801	19	18432141	<i>PDE4C</i>	0.1
rs4808801	19	18432141	<i>SSBP4</i>	$5.2 \times 10^{-4}$
rs4808801	19	18432141	<i>FKBP8</i>	0.1
rs527616	18	22591422	<i>CHST9</i>	0.08
rs3903072	11	65339642	<i>CATSPER1</i>	0.06
rs3760982	19	48978353	<i>ZNF283</i>	0.05
rs3760982	19	48978353	<i>ZNF45</i>	$7.7 \times 10^{-3}$
rs3760982	19	48978353	<i>ZNF222</i>	0.01
rs132390	22	27951477	<i>KREMEN1</i>	0.04
rs2236007	14	36202520	<i>PAX9</i>	0.01
rs6472903	8	76392856	<i>HNF4G</i>	0.07

## Supplementary Note

### iCOGS SNP Selection

SNPs were selected for the iCOGS custom genotyping array separately by each participating consortium. Each consortium was given a share of the array: nominally 25% of the SNPs each for BCAC, PRACTICAL and OCAC; 17.5% for CIMBA; and 7.5% for SNPs of general interest (“COMMON”). In practice the allocations were larger as a result of overlaps. The allocation for each consortium was divided into three categories: “GWAS replication”, “fine-mapping” and “candidate SNPs”. The GWAS replication consisted of a series of lists of SNPs identified from each of several analyses (see iCOGS website for a full description of the lists).

In general, we considered only SNPs with an Illumina design score of 0.8 or greater (some OCAC and CIMBA SNPs with lower design scores were included). Where possible, preference was given to SNPs previously genotyped by Illumina (design score 1.1). For each category, we defined a series of ranked lists of SNPs. For the GWAS SNPs, these were merged in the following way, in order to generate a single list. We selected SNPs in priority order from each list, according to predefined weightings. Where a SNP (or a surrogate) was selected on the basis of more than one list, the SNP counted towards the tally for each list. For each SNP, we preferentially accepted the SNP if it had a design score of 1.1 (i.e. had previously been genotyped on an Illumina platform). If not, we sought SNPs with  $r^2=1$  with the selected SNP, and selected the SNP with the best design score. If no such SNP was available, we selected SNPs with  $r^2>0.8$  with the chosen SNP, and selected the SNP with the best design score. We excluded SNPs which were in strong LD with a previously selected SNP ( $r^2>0.9$ ). However, for SNPs that were highly significant in each list ( $P<.00001$ ), we required two surrogate SNPs. The candidate lists were merged in the same way, giving equal weight to lists from each study. The only differences were (a) there was no provision for additional surrogates (b) SNPs were excluded if there was an existing surrogate at  $r^2=1$ .

To merge the three categories, we first included all the selected fine-mapping SNPs, and then included SNPs from the merged GWAS and candidate lists in priority order. COMMON SNPs were selected in a similar way.

Finally, lists from each of the constituent consortia were merged, in priority order and in proportion to their allocated shares. SNPs selected by one consortium and subsequently selected by another counted towards both lists. The process continued until the maximum 240,000 attempted beadtypes

had been reached. The final list comprised 220,123 SNPs. Of these, 211,155 were successfully manufactured on the array.



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